Attentional bias modification in substitute-prescribed opiate users and control participants

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D.Clin.Psy. Thesis (Volume 1), 2013

University College London

UCL Doctorate in Clinical Psychology

Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

This thesis investigated biases in the implicit processing of substance-related cues in substance users. Part 1, a literature review, assessed the effectiveness of attempts to modify such processes and the wider benefits of doing so. The 12 studies reviewed, addressing between them attentional bias, implicit attitudes and approach bias in either alcohol drinkers or tobacco smokers, suggest that implicit processes are readily modifiable. However, the evidence of wider benefit is less clear. The clinical implications and future research considerations are discussed.

Part 2 is an empirical paper, conducted jointly with a fellow trainee clinical psychologist, which assessed the effects of attentional bias modification (ABM) in opiate dependent and non-substance using control participants. Baseline differences in attentional bias (AB) between these groups were assessed, as were the effects of ABM on AB and craving. The role of treatment adherence (i.e. whether or not an individual was using illicit opiates on top of their prescribed substitute) was also explored. Contrary to predictions, there were no baseline group differences in AB, and ABM had no significant effects on AB or craving. However, treatment adherence was an important factor, with differences found between opiate dependent participants using on top, not using on top and control participants on measures of AB, craving and psychopathology. The clinical and research implications of these differences are discussed.

Finally, Part 3, the critical appraisal, provides reflections on the entire research process. Some guidance and recommendations are also offered to future researchers covering areas such as the difficulties in recruiting from these clinical populations, and possible alternative approaches to the problem of biases in implicit processes in substance use.

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Acknowledgements

I would like to thank Clare Wellington for her help and support throughout the entire process of completing this thesis. Similarly, I would like to thank Claire Mokrysz for her help in recruitment and testing of research participants, and Dr Tom Freeman for his expertise in programming the computer tasks used in the research.

In addition, I would like to thank Prof Valerie Curran and Dr Dominic O'Ryan for their tireless provision of expertise, supervision and guidance over the past few years.

Finally, I am very grateful to all of the participants who took part in the research, as well as to the staff of services in which the research took place.

Part 1: Literature Review

The modification of implicit processes in substance users: a review

Abstract

Aim: This review examined whether interventions that aim to modify implicit processes in substance users significantly alter them, and whether there is any additional clinically relevant benefit of such interventions.

Method: Studies were included if they (a) primarily aimed to modify any facet of implicit cognition in individuals who use substances, (b) assessed the effects of the intervention on at least that same facet of implicit cognition, and (c) assessed the effects of the intervention on clinically relevant outcomes. Twelve studies were selected for review.

Results: Eleven of the 12 studies reviewed found that the intervention produced significant change in the predicted direction on the implicit process it targeted. Evidence of any additional benefit of intervention was mixed. In community samples, interventions targeting implicit attitudes and approach bias produced significant change in clinically meaningful outcomes, although some findings were suggestive of a protective effect of intervention against repeated exposure to substance-related stimuli. Results of the two studies targeting attentional bias and approach bias in clinical samples were positive, with some evidence of the intervention influencing treatment outcome.

Conclusion: Interventions targeting implicit processes show promise in bringing about change in substance use behaviour. Benefits are perhaps most evident for clinical populations. However, the research is in its infancy and to date includes only two studies with clinical populations, and only alcohol and tobacco users have been examined. Replication of current findings is therefore needed, and further research should also aim to examine users of other substances, determine the benefits of single versus multiple intervention sessions, and determine whether these interventions can serve a protective role in at-risk populations.

1. Introduction

In the UK, substance use is common, with over a third of adults reporting having ever taken an illicit substance in their lives, and 5.2% having taken at least one in the past month (Health and Social Care Information Centre (HASCIC), 2012a). These figures are much higher for legal substances such as alcohol (with 68% of men and 54% of women reporting drinking in the past week; HASCIC, 2012b) and tobacco (with 20% of adults reporting regular smoking; HASCIC, 2012c). Furthermore, substance use and misuse represents a significant burden on the National Health Service (NHS), with alcohol use costing the NHS approximately £2.7bn in 2006/7 (Department of Health (DH), 2008), and tobacco use costing approximately £5.2bn in 2005/6 (5.5% of total healthcare costs; Allender, Balakrishnan, Scarborough, Webster & Rayner, 2009).

Given the harm substances can cause on the individual as well as society, the UK government has specific drug (Home Office, 2010), alcohol (Home Office, 2012) and tobacco (DH, 2011) strategies. However, substance misuse services continue to report relatively low success rates, with only 13% of adults leaving treatment dependency free in 2011-2012 (National Treatment Agency for Substance Misuse, 2012).

Substance use, misuse and dependence have consequently attracted much research. Substance use has come to be understood as a complex phenomenon, and our understanding of the multiple factors involved in its development and maintenance has gradually improved. Over the past 15 years, the importance of cognitive processes in substance use has become apparent. Therefore, models of substance use and dependence have attempted to accommodate both the traditional biological and more recently acknowledged cognitive processes. The most recent

models are known as dual process models (e.g. Deutsch & Strack, 2006; Wiers et al., 2007). A detailed description of these models is beyond the scope of this article so a brief outline only will be provided here, but interested readers can see Wiers and Stacy (2006a) for a summary, or Wiers and Stacy (2006b) for a more detailed account.

Dual process models were developed to explain the paradoxical behaviour that is repeated substance use, i.e. the fact that individuals continue to take substances despite their awareness of the risks and consequences of doing so. Therefore, purely 'rational' explanations of substance use are considered insufficient. While individual models differ in terms of their specific details, they generally include two systems, "implicit" and "explicit", as involved in substance use. The implicit system is relatively automatic, fast and associative, and includes processes such as attentional bias, motivational and affective memory associations, and approach bias. The explicit system, is slower, more rational and under conscious control. It therefore includes executive functions such as decision-making, emotion regulation, and response inhibition.

The models propose that dependence develops as the result of the emergence of an imbalance between the two systems over time: an increase in the predominance of implicit processes (leading to increased salience and motivation to use substances), accompanied by a decrease in explicit control of such implicit processes. As dependence develops, executive processes weaken and the behaviour becomes increasingly stimulus driven and implicit processes dominate, meaning substance use can be increasingly triggered by factors outside conscious awareness.

This increasing predominance of implicit processing is compatible with incentive-sensitization theory (Robinson & Berridge, 1993), which outlines the

neurobiological adaptations that underpin addiction. These adaptations are thought to give rise to attentional bias leading to motivation to use the drug and subsequent activation of approach behaviours (Robinson & Berridge, 2003, 2008). Noteworthy is that both attentional bias and approach bias (a precursor of approach behaviour) are major features of the implicit system in dual process models.

However, individual differences are important in determining one's susceptibility to developing dependence. For instance, trait impulsivity has been found to predict later addictive behaviour (e.g. de Wit, 2009) and Robinson and Berridge (1993) posit a moderating role of impulsivity in their theory. Moreover, the effect of implicit processes on behaviour is weaker in individuals with good executive control, and vice versa (Grenard et al., 2008; Houben & Wiers, 2009; Thush et al., 2008).

It would seem then that implicit and explicit processes are interrelated phenomena and are not entirely independent of one another in their involvement in substance use. Indeed, a recent meta-analysis of the alcohol literature supports this. Reich, Below and Goldman (2010) found that while implicit and explicit measures predict some shared variance in drinking behaviour, each also make a significant unique contribution. This therefore lends support to dual-process models and means it is worthwhile addressing implicit as well as explicit processes in both theoretical accounts and treatment strategies.

Current psychosocial treatments for substance misuse, however, almost exclusively target explicit cognition alone. For example, contingency management (e.g. Petry, 2006; an approach recommended by the National Institute for Health and Clinical Excellence, 2007), involves the explicit reinforcement of specified behaviours such as reduced substance use. While the evidence-base for some

psychosocial treatments is strong, it is possible that the effectiveness of interventions could be enhanced by the addition of an implicit component.

Recent evidence in mood and anxiety disorders suggests that this might indeed be possible, with favourable clinical outcomes for participants receiving interventions targeting implicit processes. For example, Hazen and colleagues (2009) found that an intervention aimed at reducing attentional bias (attentional training) in pathological worriers successfully reduced their worry as well as other anxiety symptoms. Similar beneficial effects of attentional bias interventions have been reported in generalised anxiety disorder (GAD) (Amir, Beard, Burns & Bomyea, 2009), where only 50% of patients who received the attentional training continued to meet diagnostic criteria for GAD following training compared with 87% of the control group. In addition, positive outcomes have been reported in social anxiety (Schmidt, Richey, Buckner & Timpano, 2009; Amir et al., 2009). Here, Schmidt and colleagues (2009) found a similar result to Amir, Beard et al. (2009), where again, fewer participants in the attentional training group than the control group met diagnostic criteria for social anxiety at four-month follow-up (38% and 87% respectively). There is also evidence that such interventions may act as a protective factor against depression in individuals who have experienced two or more depressive episodes in the past (Browning, Holmes, Charles, Cowen & Harmer, 2012).

Following the relative promise of implicit approaches in anxiety and mood disorders, research has begun to examine the effects of similar interventions in substance using populations. This review therefore aimed to examine this research to date. Specifically, it sought to address the extent to which: (a) interventions aimed at modifying implicit processes can significantly alter them, and (b) there is any

additional clinical benefit of such interventions, as evidenced by, for example, reduction in cravings or frequency of substance use.

2. Method

2.1 Literature search

The literature search included the PsycINFO, PubMed, Medline and Embase databases. Broadly speaking, two categories of keywords were used in the search. The first category included terms related to implicit cognition and existing techniques thought to alter implicit cognition. The second category related to substance use. The results were limited to papers in scientific, peer-reviewed and English language journals, only. A copy of the full search terms used can be found in Appendix A.

2.2 Inclusion criteria

In order to be selected, a study had to (a) employ a method that primarily aimed to modify any facet of implicit cognition in individuals who use substances, (b) assess the effects of that intervention on at least that same facet of implicit cognition, and (c) assess the effects of the intervention on other, clinically meaningful outcomes (e.g. cravings, substance use etc.).

2.3 Study selection

Following the removal of duplicates, the search returned 398 papers. The titles and abstracts of those papers were then read and checked against the inclusion criteria above. 379 papers were removed following this check. The remaining 19 papers were then read in full to finalise the study selection. Following this round of

checks, a further eight studies were removed primarily because the explicit aim of the intervention was not to modify an aspect of implicit cognition. Reference lists of the remaining 11 papers were also checked for any additional relevant studies and this revealed one further paper that was not found in the original literature search. Twelve papers in total were therefore selected for review.

3. Results

Table 1 summarises the key characteristics of the studies included. As can be seen, to date, studies employing methods aimed at modifying implicit biases have largely targeted attentional bias (eight studies), but more recently there have been approaches targeting alternative implicit processes (implicit attitudes: two studies; approach bias: two studies). Nine studies focused on alcohol users, and three studies on tobacco smokers. Only two studies to date have been conducted using a clinical sample, whereas the remainder recruited community samples with most of these examining university student populations.

The quality of each study was assessed systematically using a critical appraisal tool developed by Downs and Black (1998). This checklist is a 27-item measure spanning five areas, namely the quality of reporting ('reporting'; 10 items), the generalisability of the study ('external validity'; 3 items), bias in the intervention(s) and outcome measure(s) ('bias'; 7 items), bias in sampling or group allocation ('confounding'; 6 items), and statistical power ('power'; 1 item). An overall 'Quality Index' score is calculable, which represents the total score obtained across all items. The checklist has been shown to generally have good statistical properties, although the external validity subscale had poor reliability (Downs & Black, 1998).

Table 1
Key characteristics of the studies included in the review

Authors	Sample Size	Substance	Sample type	Implicit cognition targeted	Intervention technique	Follow-up period
Attwood et al. (2008)	55	Tobacco	University[a]	Attentional bias	Modified visual probe	None
Fadardi & Cox (2009)	160	Alcohol	Community	Attentional bias	Modified Stroop	3 months[b]
Field et al. (2007)	60	Alcohol	University[a]	Attentional bias	Modified visual probe	None
Field et al. (2009)	72	Tobacco	University[a]	Attentional bias	Modified visual probe	None
Field & Eastwood (2005)	40	Alcohol	University[a]	Attentional bias	Modified visual probe	None
Houben, Havermans & Wiers (2010)	116	Alcohol	University Students[c]	Attitudes/ affective associations	Evaluative conditioning	1 week[b]
Houben, Schoenmakers & Wiers (2010)	88	Alcohol	University Students[d]	Attitudes/ affective associations	Evaluative conditioning	1 week[b]
McHugh et al. (2010)	64	Tobacco	Community	Attentional bias	Modified visual probe	None
Schoenmakers et al. (2010)	43	Alcohol	Clinical	Attentional bias	Modified visual probe	3 months[e]
Schoenmakers et al. (2007)	106	Alcohol	University Students[d]	Attentional bias	Modified visual probe	None
Wiers et al. (2011)	214	Alcohol	Clinical	Approach bias	Approach/ avoidance task	1 week and 1 year[f]
Wiers et al. (2010)	42	Alcohol	University Students[d]	Approach bias	Approach/ avoidance task	None

[a] Sample consisted of staff and students at a university
[b] Alcohol consumption was monitored over follow-up period
[c] All participants were assessed via the internet
[d] The sample was male only
[e] Data gathered at follow-up were treatment outcome and drinking behaviour only
[f] Approach bias was assessed at 1 week follow-up, and alcohol and other substance use was assessed at 1 year follow-up

For its use in the present review, the scoring of item 27 (relating to statistical power) was modified so that studies scored either ‘0’ or ‘1,’ and studies with statistical power equal to or greater than 80% were awarded a score of ‘1’. Consequently, the Quality Index was scored out of a total of 28 points, as opposed to

the originally intended 32 points. The full item score was awarded for any individual item which was not applicable to a study.

Table 2 displays the scores obtained on the checklist by each study. The specific strengths and weaknesses of any study highlighted by the checklist will be discussed in detail under the relevant section below.

Table 2
Scores obtained by each study on the Downs & Black (1998) critical appraisal tool

	Downs & Black subscales					
Authors	*Reporting (max=11)*	*External validity (max=3)*	*Bias (max=7)*	*Confounding (max=6)*	*Power (max=1)*	*Total (max=28)*
Attwood et al. (2008)	9	1	6	5	1	22
Fadardi & Cox (2009)	9	1	3	2	1	16
Field et al. (2007)	10	1	7	6	1	25
Field et al. (2009)	8	1	7	6	1	23
Field & Eastwood (2005)	8	1	6	5	1	21
Houben, Havermans & Wiers (2010)	9	0	4	4	1	18
Houben, Schoenmakers & Wiers (2010)	8	1	5	4	1	19
McHugh et al. (2010)	10	3	6	5	1	25
Schoenmakers et al. (2010)	11	3	5	5	1	25
Schoenmakers et al. (2007)	11	1	6	5	1	24
Wiers et al. (2011)	9	3	7	6	1	26
Wiers et al. (2010)	11	1	6	5	1	24

3.1 Attentional bias

Attentional bias (AB) is the phenomenon whereby disorder-related stimuli implicitly grab one's attention. AB has consistently been found in individuals who use substances (see Field & Cox, 2008), and features as an important part of many models of addiction (e.g. Franken, 2003; Ryan, 2002; Wiers et al., 2007; Wiers & Stacy, 2006b). Eight studies reviewed here have attempted to modify AB in substance users. This has been achieved by either the modified visual probe paradigm, or the modified Stroop task.

3.1.1 Modified visual probe paradigm

Seven studies employed the modified visual probe paradigm to modify attentional bias (Attwood, O'Sullivan, Leonards, Mackintosh & Munafò, 2008; Field et al., 2007; Field, Duka, Tyler & Schoenmakers, 2009; Field & Eastwood, 2005; McHugh, Murray, Hearon, Calkins & Otto, 2010; Schoenmakers et al., 2010; Schoenmakers, Wiers, Jones, Bruce & Jansen, 2007).

This method follows MacLeod et al. (2002), and while the exact specifications of the tasks used in each study have varied, the basic principle has remained unchanged. In this task, participants are presented with two images on the screen: one a substance-related image, the other a matched neutral image. The images are followed by a probe – which may, for example, be a single or double pixel – which appears in the location of one of the images, and participants must identify the probe type as quickly and accurately as possible by pressing one of two response keys (see *Figure 1* for a representation of a single trial). In the standard version of the visual probe task, which measures AB, probes replace substance-related and neutral images equally often. AB is then determined by comparing

reaction times to the probe when it replaced the substance-related images versus the neutral images. AB for a substance would be found where participants are significantly faster to respond to the probe when it replaces the substance-related images. In the modified version of the task, where AB is *trained* (hereafter referred to as attentional bias modification; ABM), the contingency of probe location is adjusted so that the probe replaces one type of image more often than the other. For example, to train attention *away* from substances, one would replace the neutral images with probes, so that in order to improve at the task and become faster, participants should direct their attention toward the neutral stimuli, rather than the substance-related stimuli.

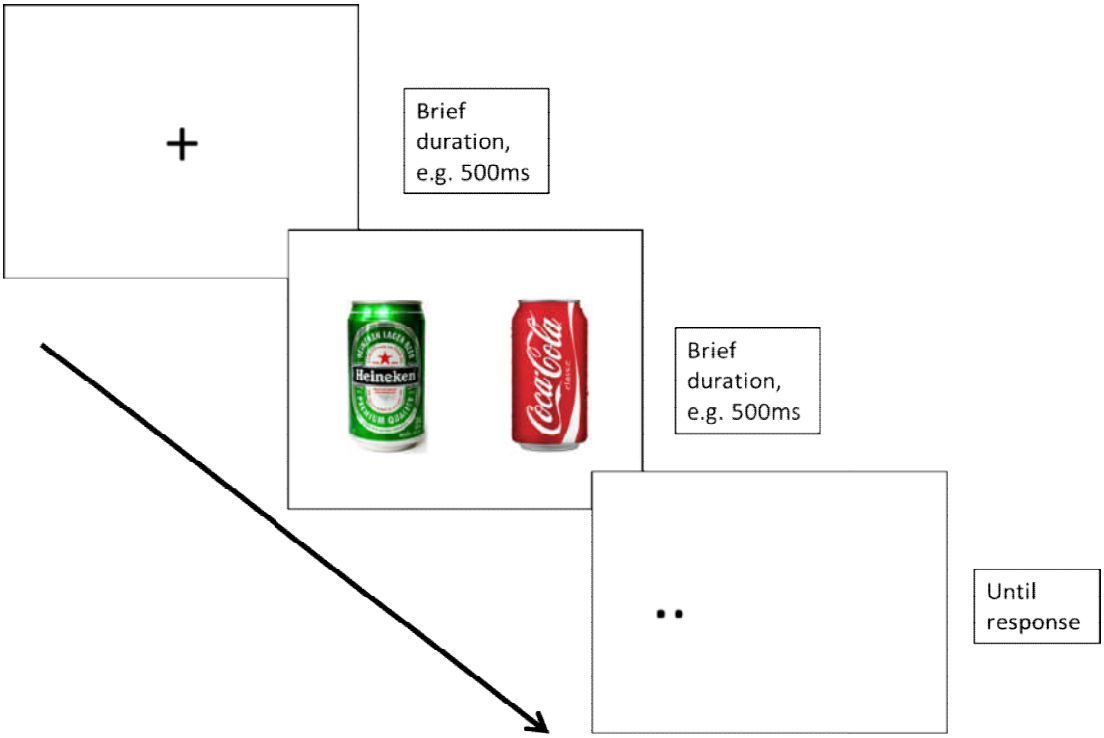

Figure 1: A visual representation of the sequence of events in a single trial of the modified visual probe task.

3.1.1.1 ABM in alcohol users

Four studies (Field et al., 2007; Field & Eastwood, 2005; Schoenmakers et al., 2010; Schoenmakers et al., 2007) employed this methodology with alcohol users,

with one study targeting a clinical sample of alcohol dependent patients (Schoenmakers et al., 2010), and the remainder investigating predominantly student alcohol drinkers. For comparison, the reported level of alcohol consumption by participants in each of these studies is given in Table 3. While there is no doubt participants in Schoenmakers and colleagues' (2010) clinical sample were drinking at very high and harmful levels, the level of drinking in the other studies' samples was much closer to recommended limits (14 UK units for women and 21 UK units for men; DH, 2005). Indeed, in the original papers, although the range of the data was not always provided and the data were not broken down by gender, on balance the data in Table 3 suggest that the majority of participants in the non-clinical samples were consuming alcohol at levels towards the lower end of the 'hazardous' range (defined as 15-35 UK units for women, 22-50 UK units for men; DH, 2005).

Table 3

Weekly alcohol consumption of participants in the four modified dot-probe ABM studies recruiting alcohol drinkers

	Sample Type	**Mean (SD) weekly alcohol consumption by group**		
		Attend Alcohol	*Avoid Alcohol*	*Control*
Field et al. (2007)	University[a]	21.73 (34.21)	22.05 (23.21)	25.63 (58.76)
Field & Eastwood (2005)	University[a]	27.65 (12.54)	25.80 (11.76)	–
Schoenmakers et al. (2010)	Clinical	215.6 (16.7)[b]	–	252.7 (28.8)[b]
Schoenmakers et al. (2007)	University Students[c]	50.2 (Range: 26.3-118)	–	50.2 (Range: 26.3-109)

Note: Values are Mean (SD), unless otherwise stated. Alcohol consumption is expressed in UK units. Data originally not in these units have been converted for comparative purposes.

[a] Sample consisted of staff and students at a university.

[b] Data provided in paper are for mean *daily* consumption for single day prior to admission for treatment. For comparative purposes, value given in the table is estimated, and was calculated by multiplying by seven the mean daily consumption figures.

[c] The sample was male only.

Across all four studies, ABM aimed at training attention away from alcohol-related stimuli successfully reduced AB immediately following the intervention. However, evidence of additional clinical benefit in these 'avoid alcohol' ABM groups was very limited, with only Schoenmakers et al. (2010) reporting any such benefit. In their clinical sample, the ABM intervention produced generalisation to novel stimuli (a finding not found in Field et al., 2007, or Schoenmakers et al., 2007) and participants in this group were also discharged from treatment significantly earlier than participants in the control group. The other three studies failed to find any further benefit of ABM aimed at training attention away from alcohol-related stimuli. Noteworthy, however, was the 'adverse' effects apparent in those studies employing a 'toward alcohol' control group (i.e. attentional training away from neutral and towards alcohol-related stimuli). Two of the studies included such control groups, and found that it increased participants' urge to drink (Field & Eastwood, 2005; Field et al., 2007) and led to greater alcohol consumption upon a taste test (Field & Eastwood, 2005, only). Furthermore, Field and colleagues (2007) found that the training effect in this control group generalised to novel alcohol stimuli; a finding not found in other groups in the same study or in other studies (with the exception of Schoenmakers et al., 2010; see above).

The scores obtained by each paper upon critical appraisal (see Table 2) suggest that in general, all four studies were well designed and well reported. The three studies using community samples fared poorly on external validity, due to the fact that they recruited a largely university student sample and one study (Schoenmakers et al., 2007) recruited men only.

The appraisal highlighted the role of blinding and contingency awareness in research of this type. Schoenmakers et al. (2010) explicitly informed participants in

the ABM group that probes would never appear behind alcohol-related images. As a result, this study had a reduced score on the bias subscale of the appraisal checklist. In the three other studies, however, no explicit instruction was given and, instead, awareness was assessed after the study had been completed. Field and Eastwood (2005) and Schoenmakers et al. (2007) found that awareness in any group did not affect any of the results. Field et al. (2007), however, did note that awareness was important in the 'attend alcohol' control group where aware participants experienced increased craving for alcohol during a taste test. Therefore, awareness was generally found to be rare and important perhaps only in the control conditions.

Noteworthy is that the variation in the findings between Schoenmakers et al. (2010) and the three other studies may be attributable to the two major differences in their design and nature. First, Schoenmakers et al. (2010) used a clinical sample. Second, participants in that clinical sample were exposed to multiple sessions of ABM, as opposed to a single session as in the other three studies. This issue will be discussed further in section *4.1*, below.

3.1.1.2 ABM in tobacco smokers

A further three studies (Attwood et al., 2008; Field et al., 2009; McHugh et al., 2010) employed the modified visual probe methodology in tobacco smokers. McHugh et al. (2010) recruited a community sample, while Attwood et al. (2008) and Field et al. (2009) recruited a predominantly university student sample. Only two studies found an effect of ABM on AB in the predicted directions (Attwood et al., 2008; Field et al., 2009). However, there were no reported additional beneficial effects of ABM in the experimental groups in either study (i.e. no generalisation to novel stimuli, no reduction in craving or changes in behavioural measures of

smoking). A similar 'adverse' effect in the 'attend tobacco' control group to that found in the studies with alcohol users (see section *3.1.1.1*, above) was reported by Attwood et al. (2008). However, this effect was gender specific, where only men in this group experienced greater cravings during a smoking exposure test. Such a gender effect has not been reported since, however, including by Field et al. (2009) who specifically examined this in their analyses.

All three studies fared well upon critical appraisal (see Table 2), with external validity being the main issue for Attwood et al. (2008) and Field et al. (2009) given that their samples were largely drawn from a university student population. While McHugh et al. (2010) scored well upon appraisal and indeed was sufficiently powered to detect a significant effect, close examination of the intervention itself raises possible reasons as to why the authors found no effect of ABM. First, in their experimental group, probes replaced neutral stimuli on only 85% of trials. While some studies have chosen to not use a 100% contingency, most studies do not use below 90%; indeed, both Attwood et al. (2008) and Field et al. (2009) used 100% contingencies. Second, their probe consisted of a single dot which replaced either the top image or the bottom image, and participants needed only to indicate its location. The problem here is that this requires minimal attentional resources, as it is possible for participants to detect the location of the probe by using their peripheral vision alone. No other ABM study covered in this review that employed the modified visual probe paradigm used this probe type, and indeed, all other studies found a significant effect of ABM on AB at the very least.

3.1.2 Modified Stroop paradigm

One study (Fadardi & Cox, 2009) employed this methodology to modify AB in a community sample of alcohol users. In relation to substance use, the Stroop task

consists of substance-related or neutral words presented one at a time, which appear in one of a few different coloured fonts. As quickly and accurately as possible, participants are requested to name the font colour (while ignoring the word). The difference in reaction time to name the font colours of substance-related and neutral words is analysed, and participants who are slower to respond on substance-related items are said to have an AB toward those stimuli.

Fadardi and Cox (2009) modified this classic Stroop interference task and created the Alcohol Attention-Control Training Program (AACTP). Rather than words, the task uses images of alcoholic and soft drinks, and runs in three progressively more difficult series. In series one and two, images are displayed individually with a coloured background (series one) or coloured outline (series two), and participants are required to name the colour of the outline/background as quickly as possible. In the third series, an alcoholic and soft-drink stimulus are presented side by side, each with a coloured outline, and participants must determine the colour of the outline of the soft-drink stimulus (for full details of the task, see Fadardi and Cox, 2009). In addition, although the AACTP addresses an implicit cognitive process (AB), it is explicit in its aim, with its rationale explained to participants and feedback on performance provided (with a view to enhancing participants' motivation).

For the training component of the study, the sample consisted of 68 hazardous drinkers (19 male, mean alcohol consumption = 47.91 (*SD* = 33.00) UK units per week; 49 female, mean alcohol consumption = 41.38 (*SD* = 27.67) UK units per week) and 92 harmful drinkers (80 male, mean alcohol consumption = 59.70 (*SD* = 42.48) UK units per week; 12 female, mean alcohol consumption = 83.33 (*SD* = 48.90) UK units per week) recruited from a university and community population. The study assessed the AACTP's effect on AB (both groups), as well as

on actual alcohol consumption (harmful drinkers only). The authors reported a good outcome, with the AACTP successfully reducing AB for alcohol in both groups, and with the harmful drinkers also showing reductions in alcohol consumption (maintained at 3-month follow-up) and improvement on other measures (i.e. motivation to change, drinking-related locus of control, positive affect and situational confidence). However, while these findings were statistically significant, it is difficult to determine the true size and meaningfulness of the change in these outcomes. For example, since alcohol consumption over time is represented only in a figure and additional, accurate post-training data are not provided, it is difficult to determine if, for instance, harmful drinking participants' alcohol consumption changed to the extent that they could be reclassified as hazardous drinkers (a clinically less harmful level of drinking (DH, 2005)).

However, as can be seen in Table 2, the study fared poorly upon critical appraisal. In particular, it scored poorly on the subscales of confounding and bias. The major methodological issue was that the study did not include a control group. Instead, harmful drinking participants acted as their own controls, by waiting one month before beginning the intervention. While it was indeed true that the participants in the harmful drinking sample did not change on key measures during the waiting period, caution must be used when interpreting the results. In addition, drop-out rates were very high in the harmful drinking group (45.7% by follow-up), yet this was not accounted for in the data analysis by, for example, the use of an intention to treat analysis.

Hazardous drinkers also had no control group. This group were given two sessions of training, one week apart, and their AB was measured before the first and after the second training sessions. With this design, it is unclear whether two sessions

of training were necessary to modify AB since there was no assessment of AB at any time point between training sessions i.e. the effects of training may have worn off within a week, but the second training session led to a change in AB at the final assessment.

In addition, it was not clear exactly what data were included in main analyses. For example, under the analyses for hazardous drinkers (who should drink, on average, between 22-50 units/week for men or 15-35 units/week for women; DH, 2005), the mean number of units of alcohol consumed for the "high" alcohol consumption subgroup was quoted as 75.75 (*SD* = 20.35) units, which is well in excess of the upper limit for this group. The opposite problem was evident in analyses for harmful drinkers' data, where the "low" alcohol subgroup consumed on average just 14.30 (*SD* = 3.35) units per week (which is within safe limits).

A further methodological issue comes with the use of the Stroop task itself. There is recent evidence to suggest that factors other than attentional bias can cause interference on the task, such as the words eliciting subjective craving which in turn increases cognitive load and therefore leads to interference (Tiffany, 1990), a general slowing of responding when emotionally salient stimuli are presented (Algom, Chajut & Lev, 2004), or by participants' attempts to suppress their distraction by substance-related stimuli (Klein, 2007). It is therefore difficult to infer causality from studies that employ this methodology.

Taken together, the methodological problems and lack of clarity in reporting of data means it is difficult to reliably ascertain the effects of the AACTP without further, more stringent, research.

3.2 Implicit attitudes

Two studies (Houben, Havermans & Wiers, 2010; Houben, Schoenmakers & Wiers, 2010) targeted implicit attitudes. Implicit attitudes can be defined as unconscious or automatic affective associations. It is held that these positive implicit attitudes develop primarily through classical conditioning principles, where a substance-related stimulus is repeatedly paired with positive affect (e.g. Olson & Fazio, 2001). The two studies under review here employed evaluative conditioning (EC) which rests on the same classical conditioning principles, whereby its aim is to repeatedly pair substance-related stimuli with *negative* affect so as to modify the attitude the individual holds. To use an example of alcohol, in order to modify implicit attitudes to make them more negative towards alcohol, participants would see alcohol-related words (e.g. “wine”, “beer”) paired consistently with pictures of negative facial expressions. In control conditions, alcohol-related words would be paired consistently with pictures of neutral facial expressions.

Both studies tested relatively large samples of students who drink alcohol (see Table 1), with Houben, Schoenmakers and Wiers (2010) recruiting males only (who consumed 24.6 (*SD* = 2.49) UK units per week on average at baseline), and Houben, Havermans and Wiers (2010) recruiting a mixed sample, although it was predominantly (76%) female (who consumed 13.1 (*SD* = 14.59) UK units per week on average at baseline). Both studies reported positive outcomes, with participants in experimental conditions showing more negative attitudes towards alcohol following EC (an effect was found on implicit attitudes in Houben, Havermans & Wiers (2010), and explicit attitudes in Houben, Schoenmakers & Wiers (2010)), and consuming less alcohol at one week follow-up (both studies). In addition, Houben, Schoenmakers and Wiers (2010) also reported that participants in the experimental

group reported fewer cravings for alcohol and consumed significantly less alcohol during a taste test (87.31ml (*SD* = 56.59) consumed in the experimental condition versus 118.43ml (*SD* = 56.55) in the control condition).

The two studies differed in their methodology and design, each with its own strengths and weaknesses. As can be seen in Table 2, both studies had weaknesses, particularly with confounding and external validity. The results of both studies are difficult to generalise given their selective samples of students with clear gender bias. Houben, Schoenmakers and Wiers (2010) used a covert design, where steps were taken to conceal the aims of the study from participants. While this was successful (participants remained unaware of the aims of the study), it prevented the measurement of attitudes at baseline. Therefore, while differences in explicit attitudes were reported after EC, it is not known whether there were baseline differences between groups in these attitudes which might explain this finding. Houben, Havermans and Wiers (2010) successfully captured key variables at baseline. However, testing of participants was conducted via the internet, raising possible questions of the participants' motivation and effort during testing. While the authors cited a prior study validating the use of web-based administration of similar tests (Houben & Wiers, 2008a), this study did not validate the use EC paradigms online, and at some stage in that cited study all participants met with the researchers in person, which was not the case in the study under review here. A final weakness of the Houben, Havermans and Wiers (2010) study, as the authors acknowledge and discuss, is that there were significant baseline differences between groups in alcohol consumption and in implicit and explicit attitudes. Taken together, these weaknesses make meaningful interpretation of the findings extremely difficult.

3.3 Approach bias

Two studies (Wiers, Eberl, Rinck, Becker & Lindenmeyer, 2011; Wiers, Rinck, Kordts, Houben & Strack, 2010) targeted approach bias. Approach bias is characterised as an action tendency, which can be triggered by substance-related stimuli in substance users. The two studies targeted approach bias in alcohol users, and both utilised the alcohol Approach Avoidance Task (aAAT). In this task, images of either alcohol-related or soft-drink stimuli appear in either landscape or portrait orientation, and participants were instructed to pull a joystick (approach movement) to one orientation, and push a joystick (avoidance movement) to the other orientation. Pulling the joystick increases the size of the picture, and pushing decreases it, therefore simulating the effects of actual physical approach and avoidance. To assess approach bias, alcohol-related and neutral images appeared equally often in both orientations, and differences in reaction times across stimuli and approach/avoidance movements are analysed to establish any approach bias towards alcohol.

The two studies employed slightly different versions of the training task, so interested readers are pointed to each paper for a detailed description. In brief, both studies implicitly trained some participants to avoid alcohol by displaying alcohol-related images in the orientation requiring an avoidance movement. Wiers et al. (2011), who also investigated the role of contingency awareness, had another training version of the task where all images were presented in a square format, but where participants were instructed to 'avoid' alcohol-related images, and 'approach' soft-drink related images.

Both studies reported positive outcomes. Wiers et al. (2010), who studied 42 male, hazardous drinking students (mean weekly alcohol consumption: ‘approach’

group = 25.5 (*SD* = 9.8) UK units; 'avoid' group = 31.9 (*SD* = 10.4) UK units), found that a single session the aAAT successfully modified approach bias (with the biggest effect in the avoid-alcohol group), which generalised to novel stimuli as well as a different test assessing automatic action tendencies (the Implicit Association Test (IAT)). Furthermore, in individuals who responded to the training intervention, there was a significant effect on a taste test, whereby participants in the avoid-alcohol group consumed significantly less alcohol (approximately 200ml less, *SD* not given) than those in the approach-alcohol group. Wiers et al. (2011) found similar results in their *clinical* sample of 214 alcoholic inpatients (currently abstinent for 3 weeks following detoxification, but with an approximate duration of alcohol dependence to that point of 12 years), with four sessions of the aAAT delivered over four days successfully changing patients' approach bias for alcohol into an avoidance bias, which again generalised to novel stimuli and to the IAT. Patients in the avoid alcohol group also tended to have improved treatment outcomes at one-year follow-up, although this finding was not quite statistically significant. Of note, very few participants became aware of the contingency in the Wiers et al. (2010) study yet the intervention was still beneficial. Furthermore, as described above, while Wiers et al. (2011) designed their study to explicitly examine the role of awareness, the groups were collapsed for statistical analysis as it was found that awareness of the contingency had no significant effect on outcome measures.

As can be seen in Table 2, both studies scored highly upon systematic appraisal. In general, both studies were well-designed and clearly reported. It is difficult to generalise the results of Wiers et al. (2010) beyond its own sample, however, as the sample size was quite small and consisted entirely of male university students. Furthermore, some group differences were evident at baseline, although

these were controlled for appropriately during statistical analysis. The significant findings of Wiers et al. (2011), however, provide some reassurance over the findings of the earlier paper.

4. Discussion

This review has covered studies which aimed to modify implicit processes that are known to be important in substance use and examined whether such approaches are effective in eliciting significant change in clinically relevant indices. Twelve such studies met the criteria for inclusion. Nine studies involved alcohol users, three involved tobacco smokers, and three different interventions were used across the studies: attentional bias modification (ABM), evaluative conditioning (EC) and the alcohol Approach Avoidance Test (aAAT).

The findings across the studies were varied. However, a consistent finding was that any attempt to modify a specific implicit process was successful in that it produced significant change in that implicit process. The only exception to this finding was McHugh et al. (2010), who used a modified visual probe task to alter AB in tobacco smokers. As discussed above, however, the variation in the specifications of the ABM task used in their study compared to those used in other similar studies likely explains its null findings.

Broader conclusions about the potential benefits of these interventions are precluded, however, as the results were variable both between and within studies addressing different implicit processes.

Studies investigating community samples have produced mixed results. Those addressing AB found no benefits of ABM aimed at avoiding substance-related stimuli beyond the modification of AB itself. There were, however, some additional

effects of ABM in control participants who were trained to *attend* to substance-related stimuli. In these groups, ABM led to an increased urge to drink (Field & Eastwood, 2005; Field et al., 2007), increased alcohol consumption during a taste test (Field & Eastwood, 2005), and increased cravings for tobacco during a smoking exposure task (Attwood et al., 2008). In fact, only one study with an '*attend* substance' control group found no such additional effects (Field et al., 2009). While these additional effects of ABM in control groups are interesting from a theoretical point of view, they offer little to the development of treatment approaches for substance using individuals.

Encouragingly, however, findings from studies addressing other implicit processes in community samples, while fewer in number, successfully produced more clinically meaningful results in their experimental 'avoid substance' groups. EC paradigms brought about decreased alcohol consumption at follow-up (Houben, Havermans & Wiers, 2010; Houben, Schoenmakers & Wiers, 2010). In addition, Houben, Schoenmakers and Wiers (2010) also found that EC led to decreased craving for – and consumption of – alcohol during a taste test. While important, further studies will be required to replicate these findings, largely due to methodological issues with each study (see section *3.2.* above for details). In addition, Wiers et al. (2010), who used the aAAT in a study with fewer methodological and design problems (see Table 2 and section *3.3*), also found that the experimental 'avoid substance' training brought about benefit beyond a change in approach bias alone, with effects generalising to novel stimuli (a finding only sometimes reported in studies targeting AB), and participants consuming significantly less alcohol during a taste test (although this only applied to participants who responded to training).

The two studies targeting *clinical* samples, although few in number, produced some promising results. Schoenmakers and colleagues (2010), for example, was the only ABM study using a modified visual probe task to provide evidence of beneficial effects beyond modification of AB, with their 'avoid substance' experimental group demonstrating generalisation of ABM effects to novel stimuli and a possible beneficial influence on treatment outcomes. In addition, Wiers et al. (2011) reported similarly promising findings with use of the aAAT, although this intervention's effect on treatment outcomes was at trend-level only. Furthermore, harmful drinkers in Fadardi and Cox's (2009) sample showed good outcomes, with a decrease in alcohol consumption and improvement on other secondary measures. However, the findings from this latter study must be considered in the context of its methodological issues (see section *3.1.2* above).

4.1 Differential effects in different populations?

Taken together, it is possible to hypothesise differential effects of interventions targeting implicit processes in different populations. For instance, such interventions may serve a protective function against repeated exposure to substance-related stimuli in *non-clinical* populations consuming relatively lower amounts of alcohol and tobacco. Houben, Havermans and Wiers (2010) discuss this with respect to their findings with evaluative conditioning (EC); it was noted that the significant difference between groups in explicit attitudes following EC was due to the control group becoming less negative in their attitudes towards alcohol, rather than the experimental group becoming more negative. They suggest that EC may therefore have acted as a buffer against the negative effects of repeated exposure to alcohol-related stimuli. It should be noted that approaches using the aAAT demonstrate early

promise in providing benefit beyond a change in approach bias alone in non-clinical populations (Wiers et al., 2010), although replication is necessary to ensure these findings are reliable and to establish whether such effects continue across a follow-up period.

On the other hand, in studies examining *clinical* samples, more clinically desirable effects are observed following interventions aimed at reducing implicit biases. Given that implicit biases are positively correlated with the degree of substance use (e.g. AB in alcohol use: Townshend & Duka, 2001; AB in heroin use: Bearre, Sturt, Bruce & Jones, 2007; AB in cannabis use: Field, 2005; implicit attitudes in alcohol use: Houben & Wiers, 2008b), it may be the case that these biases are more amenable to modification in clinical samples, and also that effects beyond change in implicit biases alone are more detectable given that scores on commonly measured outcomes in such studies are significantly higher at baseline in clinical groups seeking treatment (e.g. craving is higher, substance use is higher).

However, the studies examining clinical populations also employed multiple training sessions of the implicit intervention. It is therefore possible that it is simply multiple training sessions that is important to achieve broad benefits of training interventions. Further research is therefore necessary to establish which of these hypotheses is correct i.e. whether training interventions provide broad benefit in clinical samples and a protective effect in non-clinical samples, or whether such interventions require repeated administration to generate wider benefits. Of course, these possibilities are not necessarily mutually exclusive, and should both be true then these interventions could be useful as both protective for at-risk individuals and as a useful adjunct to treatment for clinical populations.

4.2 Awareness and motivation

A final point of discussion is the role of participants' awareness and motivation. A goal in much substance misuse treatment is to enhance an individual's motivation to change prior to beginning treatment (e.g. Motivational Interviewing; Miller & Rollnick, 2002). However, the role of motivation in the studies reviewed here has had mixed findings. On the one hand, Fadardi and Cox (2009) built feedback into their task to motivate participants to improve their performance. Importantly, while their intervention increased motivation as assessed by the Readiness To Change Questionnaire (Rollnick, Heather, Gold & Hall, 1992), their secondary analyses revealed that it was those participants who entered the study highest in adaptive motivation at baseline (as measured by the Personal Concerns Inventory (Cox & Clinger, 2002)) had the best outcomes following ABM. On the other hand, however, Wiers et al. (2011) found no difference in outcome between participants randomly assigned to either an explicit or implicit training condition i.e. attempts to inform participants of experimental contingencies and enhance their motivation made no difference to outcomes. Indeed, most studies reviewed here attempted to blind participants to the objectives of the research, and most (but not all) found that participants generally remained unaware of experimental contingencies and that contingency awareness did not significantly affect the results.

4.3 Summary

In sum, to date, research examining the impact of interventions that target implicit cognition in substance users show promise in reducing implicit processing biases and other clinically relevant outcomes. However, studies are few in number, which means broader conclusions cannot be drawn. Indeed, there have been only two

studies examining implicit interventions in clinical populations to date, and taken together the literature has only examined alcohol drinkers and tobacco smokers. While one might predict on the basis of the underlying theory that similar findings would be produced with users of other substances, the present findings cannot be generalised in this way and further research with individuals who use other substances would be necessary to confirm such a prediction. Indeed, it is likely that at least some participants in the studies reviewed here also use substances other than those targeted by the intervention (e.g. some alcohol drinkers are also likely to smoke tobacco), which therefore makes the picture more complex.

Future research should therefore aim to address the importance of single versus multiple training sessions, to clarify the importance and impact of participants' awareness and motivation, and to assess, perhaps by way of longitudinal studies, whether interventions targeting implicit cognition can have a protective or preventative effect in non-clinical populations.

5.0 References

Algom, D., Chajut, E., & Lev, S. (2004). A rational look at the emotional Stroop phenomenon: a generic slowdown, not a Stroop effect. *Journal of Experimental Psychology: General*, *133*, 323-338.

Allender, S., Balakrishnan, R., Scarborough, P., Webster, P., & Rayner, M. (2009). The burden of smoking-related ill health in the United Kingdom. *Tobacco Control*, *18*, 252-255.

Amir, N., Beard, C., Burns, M., & Bomyea, J. (2009). Attention modification program in individuals with generalized anxiety disorder. *Journal of Abnormal Psychology*, *118*, 28-33.

Amir, N., Beard, C., Taylor, C. T., Klumpp, H., Elias, J., Burns, M., & Chen, X. (2009). Attention training in individuals with generalized social phobia: a randomized controlled trial. *Journal of Consulting and Clinical Psychology*, *77*, 961–973.

Attwood, A. S., O'Sullivan, H., Leonards, U., Mackintosh, B., & Munafò, M. R. (2008). Attentional bias training and cue reactivity in cigarette smokers. *Addiction*, *103*, 1875-1882.

Bearre, L., Sturt, P., Bruce, G., & Jones, B. T. (2007). Heroin-related attentional bias and monthly frequency of heroin use are positively associated in attenders of a harm reduction service. *Addictive Behaviours*, *32*, 784-792.

Browning, M. Holmes, E. A., Charles, M., Cowen, P. J., & Harmer, C. J. (2012). Using attentional bias modification as a cognitive vaccine against depression. *Biological Psychiatry*, *72*, 572-579.

Cox, W. M., & Klinger, E. (2002). Motivational structure: relationships with substance use and processes of change. *Addictive Behaviours*, *27*, 925-940.

de Wit, H. (2009). Impulsivity as a determinant and consequence of drug use: a review of underlying processes. *Addiction Biology, 14*, 22-31.

Department of Health. (2005). *Alcohol Needs Assessment Research Project (ANARP): the 2004 national alcohol needs assessment for England*. Retrieved November 2012, from http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4122239.pdf

Department of Health. (2008). *The cost of alcohol harm to the NHS in England*. Retrieved November 2012, from http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_086421.pdf

Department of Health. (2011). *Health lives, healthy people: A tobacco control plan for England*. Retrieved November 2012, from http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_124960.pdf

Deutsch, R., & Strack, F. (2006). Reflective and impulsive determinants of addictive behaviors. In R. W. Wiers & A. W. Stacy (Eds.), *Handbook of implicit cognition and addiction* (pp. 45-57). Thousand Oaks, CA: SAGE Publishers.

Downs, S. H., & Black, N. (1998). The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology & Community Health, 52*, 377-384.

Fadardi, J. S., & Cox, W. M. (2009). Reversing the sequence: reducing alcohol consumption by overcoming alcohol attentional bias. *Drug and Alcohol Dependence, 101*, 137-145.

Field, M. (2005). Cannabis 'dependence' and attentional bias for cannabis-related words. *Behavioural Pharmacology*, *16*, 473-476.

Field, M., Duka, T., Eastwood, B., Child, R., Santarcangelo, M., & Gayton, M. (2007). Experimental manipulation of attentional biases in heavy drinkers: do the effects generalise? *Psychopharmacology*, *192*, 593-608.

Field, M., Duka, T., Tyler, E., & Schoenmakers, T. (2009). Attentional bias modification in tobacco smokers. *Nicotine & Tobacco Research*, *11*, 812-822.

Field, M., & Eastwood, B. (2005). Experimental manipulation of attentional bias increases the motivation to drink alcohol. *Psychopharmacology*, *183*, 350-357.

Franken, I. H. A. (2003). Drug craving and addiction: integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *27*, 563-579.

Grenard, J. L., Ames, S. L., Wiers, R. W., Thush, C., Sussman, S., & Stacy, A. W. (2008). Working memory capacity moderates the predictive effect of drug-related associations on substance use. *Psychology of Addictive Behaviours*, *22*, 426-432.

Hazen, R. A, Vasey, M. W., & Schmidt, N. B. (2009). Attentional retraining: a randomized clinical trial for pathological worry. *Journal of Psychiatric Research*, *43*, 627–633.

Health And Social Care Information Centre. (2012a). *Statistics on drug misuse: England, 2012*. Retrieved November 2012, from http://www.ic.nhs.uk/webfiles/publications/003_Health_Lifestyles/Statistics%20on%20drug%20misuse%202012/drug_misu_eng_2012_rep.pdf

Health And Social Care Information Centre. (2012b). *Statistics on alcohol: England, 2012*. Retrieved November 2012, from http://www.ic.nhs.uk/webfiles/publications/003_Health_Lifestyles/Alcohol_2012/Statistics_on_Alcohol_England_2012.pdf

Health And Social Care Information Centre. (2012c). *Statistics on smoking: England, 2012*. Retrieved November 2012, from http://www.ic.nhs.uk/webfiles/publications/003_Health_Lifestyles/Statistics%20on%20Smoking%202012/stats_smok_eng_2102_rep.pdf

Home Office. (2010). *Drug Strategy 2010: Reducing demand, restricting supply, building recovery: Supporting people to live a drug free life*. Retrieved November 2012, from http://www.homeoffice.gov.uk/publications/alcohol-drugs/drugs/drug-strategy/drug-strategy-2010?view=Binary

Home Office. (2012). *The government's alcohol strategy*. Retrieved November 2012, from http://www.homeoffice.gov.uk/publications/alcohol-drugs/alcohol/alcohol-strategy?view=Binary

Houben, K., Havermans, R. C., & Wiers, R. W. (2010). Learning to dislike alcohol: conditioning negative implicit attitudes toward alcohol and its effect on drinking behavior. *Psychopharmacology, 211*, 79-86.

Houben, K., Schoenmakers, T. M., & Wiers, R. W. (2010). I didn't feel like drinking but I don't know why: the effects of evaluative conditioning on alcohol-related attitudes, craving and behavior. *Addictive Behaviours, 35*, 1161-1163.

Houben, K., & Wiers, R. W. (2007). Are drinkers implicitly positive about drinking alcohol? Personalizing the alcohol-IAT to reduce negative extrapersonal contamination. *Alcohol, 42*, 301-307.

Houben, K., & Wiers, R. W. (2008a). Measuring implicit alcohol associations via the internet: Validation of web-based implicit association tests. *Behavior Research Methods, 40,* 1134-1143.

Houben, K., & Wiers, R. W. (2008b). Implicitly positive about alcohol? Implicit positive associations predict drinking behavior. *Addictive Behaviours, 33,* 979-986.

Houben, K., & Wiers, R. W. (2009). Response inhibition moderates the relationship between implicit association and drinking behavior. *Alcoholism: Clinical and Experimental Research, 33,* 626-633.

Klein, A. A. (2007). Suppression-induced hyperaccessibility of thoughts in abstinent alcoholics: A preliminary investigation. *Behaviour Research and Therapy, 45,* 169-177.

McHugh, R. K., Murray, H. W., Hearon, B. A., Calkins, A. W., & Otto, M. W. (2010). Attentional bias and craving in smokers: the impact of a single attentional training session. *Nicotine & Tobacco Research, 12,* 1261-1264.

Miller, W. R., & Rollnick, S. (2002). *Motivational interviewing: Preparing people for change* (2nd ed.). New York: Guilford Press.

National Institute for Health and Clinical Excellence. (2007). *Drug misuse – psychosocial interventions*. Retrieved November 2012, from http://publications.nice.org.uk/drug-misuse-psychosocial-interventions-cg51

National Treatment Agency for Substance Misuse. (2012). *Statistics from the National Drug Treatment Monitoring System (NDTMS), 1 April 2011– 31 March 2012, Vol. 1: The numbers*. Retrieved November 2012, from http://www.nta.nhs.uk/uploads/statisticsfromndtms201112vol1thenumbersfinal.pdf

Olson, M. A., & Fazio, R. H. (2001). Implicit attitude formation through classical conditioning. *Psychological Science, 12*, 413-417.

Palfai, T. P., & Ostafin, B. D. (2003). Alcohol-related motivational tendencies in hazardous drinkers: assessing implicit response tendencies using the modified IAT. *Behaviour Research and Therapy, 41*, 1149-1162.

Petry, N. (2006). Contingency management treatments. *British Journal of Psychiatry, 189*, 97–98.

Reich, R. R., Below, M. C., & Goldman, M. S. (2010). Explicit and implicit measures of expectancy and related alcohol cognitions: a meta-analytic comparison. *Psychology of Addictive Behaviours, 24*, 13-25.

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Research Reviews, 18*, 247-291.

Robinson, T. E., & Berridge, K. C. (2003). Addiction. *Annual Review of Psychology, 54*, 25-53.

Robinson, T. E., & Berridge, K. C. (2008). The incentive sensitization theory of addiction: some current issues. *Philosophical Transactions of the Royal Society: Biological Sciences, 363*, 3137-3146.

Rollnick, S., Heather, N., Gold, R., & Hall, W. (1992). Development of a short 'readiness to change' questionnaire for use in brief, opportunistic interventions among excessive drinkers. *British Journal of Addiction, 87*, 743–754.

Ryan, F. (2002). Detected, selected, and sometimes neglected: cognitive processing of cues in addiction. *Experimental and Clinical Psychopharmacology, 10*, 67-76.

Schmidt, N. B., Richey, J., Buckner, J. D., & Timpano, K. R. (2009). Attention training for generalized social anxiety disorder. *Journal of Abnormal Psychology*, *118*, 5–14.

Schoenmakers, T. M., de Bruin, M., Lux, I. F. M., Goertz, A. G., Van Kerkhof, D. H. A. T., & Wiers, R. W. (2010). Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. *Drug and Alcohol Dependence*, *109*, 30-36.

Schoenmakers, T. M., Wiers, R. W., Jones, B. T., Bruce, G., & Jansen, A. T. M. (2007). Attentional re-training decreases attentional bias in heavy drinkers without generalization. *Addiction*, *102*, 399-405.

Thush, C., Wiers, R. W., Ames, S. L., Grenard, J. L., Sussman, S., & Stacy, A. W. (2008). Interactions between implicit and explicit cognition and working memory capacity in the prediction of alcohol use in at-risk adolescents. *Drug and Alcohol Dependence*, *94*, 116-124.

Tiffany, S. T. (1990). A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. *Psychological Review*, *97*, 147-168.

Townshend, J. M., & Duka, T. (2001). Attentional bias associated with alcohol cues: differences between heavy and occasional social drinkers. *Psychopharmacology*, *157*, 67-74.

Wiers, R. W., Bartholow, B. D., van den Wildenberg, E., Thush, C., Engels, R. C. M. E., Sher, K. J., … Stacy, A. W. (2007). Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. *Pharmacology, Biochemistry and Behavior*, *86*, 263-283.

Wiers, R. W., Eberl, C., Rinck, M., Becker, E. S., & Lindenmeyer, J. (2011). Retraining automatic action tendencies changes alcoholic patients' approach

bias for alcohol and improves treatment outcome. *Psychological Science, 22*, 490-497.

Wiers, R. W., Rinck, M., Kordts, R., Houben, K., & Strack, F. (2010). Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. *Addiction*, *105*, 279-287.

Wiers, R., & Stacy, A. W. (2006a). Implicit cognition and addiction. *Current Directions in Psychological Science, 15*, 292-296.

Wiers, R., & Stacy, A. W. (Eds.). (2006b). *Handbook of implicit cognition and addiction*. Thousand Oaks, CA: SAGE Publishers.

Part 2: Empirical Paper

Attentional bias modification in substitute-prescribed opiate users and control participants

Abstract

Aims: Attentional bias (AB) is important in the development and maintenance of substance dependence, with links to craving, frequency of substance use, and substance misuse treatment outcome. Reducing AB for substance-related stimuli using AB modification (ABM) may therefore have important clinical benefits for substance users. This study assessed these potential benefits in an opiate dependent (patient) sample, with comparison to a non-substance using (control) group. The role of treatment adherence (i.e. whether or not an individual uses illicit opiates on top of their prescribed substitute) in patient participants was also examined.

Method: 23 patient and 21 control participants were randomised to receive either an ABM task designed to train attention *away* from substance-related stimuli (ABM-as), or a control task (ABM-n). AB and cravings were assessed immediately before and 30 minutes after ABM-as/ABM-n. AB, craving and frequency of substance use were also assessed at one-week and one-month follow-up in patient participants.

Results: ABM-as had no significant effect on AB for any of the participants, or on AB or craving over time in patient participants. However, use on top was an important factor in patient participants. Patient participants not using on top had a significantly greater AB *away* from substance-related stimuli than control participants, and significantly lower craving, depressive symptomatology, and impulsivity than patient participants who were using on top.

Discussion: Although the main hypotheses of the study were not supported, the secondary analyses around treatment adherence revealed some important findings. Specifically, the data suggested that it may be unhelpful to view opiate dependent individuals as a homogenous group since, depending on their use on top, they differed on baseline AB, craving and psychopathology. The clinical and research implications of these differences are discussed.

1.0 Introduction

Attentional bias (AB) - where disorder-related stimuli grab one's attention - has been consistently demonstrated in users of different substances when compared to non-substance users, including alcohol (e.g. Cox, Blount & Rozak, 2000; Stormark, Laberg, Nordby & Hugdahl, 2000), tobacco (e.g. Bradley, Field, Mogg & DeHouwer, 2004; Mogg, Bradley, Field & DeHouwer, 2003), cannabis (Field, Eastwood, Bradley & Mogg, 2006), cocaine (Copersino et al., 2004; Hester, Dixon & Garavan, 2006) and heroin (Constantinou et al., 2010; Fadardi & Ziaee, 2010; Franken, Kroon, Wiers & Jansen, 2000; Lubman, Peters, Mogg, Bradley & Deakin, 2000). Furthermore, AB has long been linked to subjective craving in addiction. Indeed, this link is supported by a recent meta-analysis which found a significant (albeit weak) association between AB and craving (Field, Munafò & Franken, 2009).

AB has also been linked to relapse in individuals abstaining from substance use, including heavy drinkers (Cox, Hogan, Kristian & Race, 2002), tobacco smokers (Waters et al., 2003), heroin users (Marissen et al., 2006) and cocaine users (Carpenter, Schreiber, Church & McDowell, 2006). Constantinou et al. (2010) also found that AB away from substance-related stimuli was positively correlated with length of abstinence in ex-heroin users, suggesting a link between AB and treatment progress. The results of these studies therefore suggest that AB can be either a risk factor for relapse (increased AB), or a promoter of abstinence (decreased AB).

Such findings have understandably led to the inclusion of AB in many recent theoretical models of addiction (e.g. Field, 2006; Franken, 2003; Ryan, 2002), where AB is awarded a central role in both the development and maintenance of substance use. Within these models, subjective craving and AB are interrelated phenomena, which form a positive feedback loop (i.e. there is a causal relationship between the

two), leading to increased substance use. Evidence of this causal mechanism to date seems to support this (see Field & Cox, 2008, for a review; see also Volume 1, Part 1 of this thesis). It follows, therefore, that direct manipulation of AB ought to produce meaningful changes in subjective craving, which could in turn impact on substance use behaviour.

To date, the most methodologically rigorous approach to addressing this question has been with the use of the modified visual probe task, which aims to experimentally manipulate AB (see MacLeod, Rutherford, Campbell, Ebsworthy & Holker, 2002, for a description). In the context of substance use, the task involves the presentation of two images on a computer screen: one substance-related image, and a matched neutral image. The images are followed by a probe – which may be, for example, an upwards or downwards arrow – which appears in the location of one of the images, and participants must identify the probe type as quickly and accurately as possible by pressing one of two response keys. In the standard version of the visual probe task, which measures AB, probes replace substance-related and neutral images equally often. AB is then determined by comparing reaction times to the probe when it replaced the substance-related images versus the neutral images. AB for substances is found where participants are significantly faster to respond to the probe when it replaces the substance-related images. In the modified version of the task, where AB is *trained* (hereafter referred to as AB modification; ABM), the contingency of probe location is adjusted so that the probe replaces one type of image more often than the other. For example, to train attention *away* from substances, one would always replace the neutral images with probes, so that in order to improve at the task and become faster at responding, participants should direct their attention toward the neutral stimuli, rather than the substance-related stimuli.

To date, the modified visual probe paradigm has been applied to tobacco smokers (Attwood, O'Sullivan, Leonards, Mackintosh & Munafò, 2008; Field, Duka, Tyler & Schoenmakers, 2009; McHugh, Murray, Hearon, Calkins & Otto, 2010), and to alcohol users in both community samples (Field & Eastwood, 2005; Field et al., 2007; Schoenmakers, Wiers, Jones, Bruce & Jansen, 2007) and a clinical sample (Schoenmakers et al., 2010).

All but one of these studies reported significant effects of ABM in the predicted direction on AB itself. McHugh and colleagues (2010) were the only researchers to report no effect of ABM. However, close examination of the specifications of their ABM task reveals a likely explanation for this; given that participants were required to respond to the location of probe only, their task was therefore less demanding of participants and could be completed by using peripheral vision alone. Typical ABM research requires participants to discriminate between two probe types, making the task more demanding and thus more likely to produce an effect on AB. It is therefore reasonable to assume that, on balance, ABM is successful in altering AB in tobacco and alcohol users.

Mixed findings have been reported, however, for the broader effects of ABM on subjective craving and substance use behaviour. Some studies noted ‘adverse’ effects of ABM towards substances, where such interventions increased subjective craving (Attwood et al., 2008, although in male participants only; Field & Eastwood, 2005; Field et al., 2007, although for participants aware of experimental contingencies only). Field and Eastwood (2005) further reported that participants in their ‘attend alcohol’ ABM group consumed more alcohol during a laboratory based taste test. However, in the clinically relevant ‘avoid substance’ training conditions, there have been limited reports of broader beneficial effects of ABM beyond a

change in AB itself. Indeed, only one study found such additional effects (Schoenmakers et al., 2010). In their clinical sample, Schoenmakers and colleagues found that while ABM did not have an immediate effect on subjective craving, training generalised to novel stimuli and participants in the 'avoid alcohol' group were also discharged from treatment significantly earlier than participants in the control group.

The extent to which ABM generalises to novel stimuli is also unclear on the basis of the research to date. As mentioned above, generalisation has been reported by some authors (i.e. Field et al., 2007, although in the 'attend alcohol' group only; Schoenmakers et al., 2010). However, other studies that have specifically investigated the question of generalisation have reported no such effect (Field et al., 2009; Schoenmakers et al., 2007).

In sum, AB has a central role in the development and maintenance of addiction, as evidenced by its relationship with subjective craving and its prediction of relapse. However, while the experimental manipulation of AB has produced some support for a causal relationship between AB, craving and substance use (as evidenced by increases in craving and substance use following ABM *towards* substance-related stimuli), evidence for its clinical utility is more limited, with evidence of generalisation being equivocal, and with just one study reporting clinically relevant, broader effects of ABM *away* from substances.

Noteworthy, however, is the fact that the one study that did report benefits of ABM *away* from substances was the only study to recruit a clinical sample of substance dependent, treatment-seeking patients (alcohol users; Schoenmakers et al., 2010). Given that AB is positively correlated with frequency of substance use (e.g. Bearre, Sturt, Bruce & Jones, 2007; Field, 2005; Townshend & Duka, 2001), it may

be the case that AB is more amenable to modification in clinical samples. Further, effects beyond change in AB alone are also more detectable given that scores on commonly measured outcomes (e.g. craving and substance use) are significantly higher at baseline in clinical populations. It is therefore possible that ABM may produce broader, clinically relevant effects in clinical populations, while in non-clinical populations (with weaker AB) it serves as a protective factor against exposure to substance-related stimuli. However, it should also be noted that Schoenmakers et al. (2010) was also the only study to employ multiple sessions of ABM. This therefore raises the possibility that it is simply multiple training sessions that is important to achieve broader benefits of ABM.

The current study aimed to extend the research in this area, investigating AB in an opiate dependent, clinical sample. As described above, four studies have previously demonstrated significantly greater AB towards substance-related stimuli in opiate users relative to non-users. Two such studies (Fardardi & Ziaee, 2010; Franken et al., 2000), however, have employed the Stroop task, and thus are limited by the problems with interpreting this task (Algom, Chajut & Lev, 2004; Klein, 2007; Tiffany, 1990). Another study (Lubman et al., 2000), while employing the methodologically more rigorous visual probe task, was limited in that control participants in that study consisted of staff at a substance misuse service who may themselves have an AB for substances. Constantinou et al. (2010), however, again using the visual probe task, provided good quality evidence that AB towards substance-related stimuli exists in current opiate dependent populations relative not only to control participants, but also relative to formerly opiate dependent participants. As described above, also, the authors noted a positive correlation between AB away from substance-related stimuli and length of abstinence in ex-

users of heroin. Taken together, this suggests that AB and treatment progress may be linked. However, no other study has yet addressed this possibility.

To date, modification of AB in opiate users has not been investigated. Therefore, this study aimed to examine the effects of a single session of ABM on AB, subjective craving, and frequency of substance use using a modified visual probe task in opiate dependent participants. Generalisation of ABM to novel stimuli was also examined. In addition, comparisons were also made to a non-substance using control group, and opiate dependent participants were followed up at one-week and one-month following ABM to assess its longer-term effects on craving and substance use. Specifically, we hypothesised that:

1. Opiate dependent participants would show a significant baseline AB toward substance-related stimuli relative to non-substance using participants, who would show no such bias.
2. A between subjects ABM would produce significant group differences in AB, with participants receiving ABM *away* from substance-related stimuli (the 'avoid-substance' ABM group; ABM-as) showing decreased AB for opiate-related stimuli, whereas participants receiving a standard visual probe task as a control condition (i.e. the 'neutral' ABM group; ABM-n) would show no significant change in AB.
3. Amongst opiate-dependent participants, relative to the ABM-n group, the ABM-as group would show a significant decrease in subjective craving immediately following ABM.

As part of secondary analyses, the questions of generalisation of ABM to novel stimuli and the role of awareness of experimental contingencies were addressed. In addition, given that no ABM study using the modified visual probe task

to date has examined the longer-term effects of ABM on AB itself, craving, or frequency of substance use, we also explored the effects of this single session of ABM on these outcomes at one-week and one-month follow-up amongst opiate dependent participants. Finally, given that the only previous visual probe study with an adequate control group showed that progress through treatment was an important independent variable in determining AB (Constantinou et al., 2010), in this study we also explored this by comparing those participants who adhered to opiate substitute medication only versus those who, in addition to their prescribed substitute, continued to use opiates illicitly.

2.0 Method

This was a joint study with a fellow Trainee Clinical Psychologist, Clare Wellington (see Wellington, 2013), and our sample was therefore shared. Additional assistance in data collection was provided by Claire Mokrysz, a PhD student at University College London (UCL). Appendix B sets out the specific contributions of each person to the study.

2.1 Participants

A priori power analysis was performed (using "G*Power" software; Faul, Erdfelder, Lang & Buchner, 2007) specifying alpha = 5% and desired power = 80%. Effect size estimates for the primary analysis (effect of ABM on AB) were based on Field and Eastwood (2005) and Schoenmakers et al. (2010), who quote effect sizes of d=1.27 and d=0.87, respectively. Using the latter, smaller effect size statistic, the power analysis gave a required sample size of 28 participants in total.

Two independent groups of participants were recruited: 23 current opiate users (patient group) and 21 non-substance using control participants (control group).

Participants in the patient group were required to be opiate users prescribed a substitute medication (either methadone or buprenorphine) as part of a treatment programme at a local National Health Service (NHS) substance misuse service, and have normal or corrected-to-normal vision. They were recruited via poster advertisements and/or through their key workers. Exclusion criteria were a current diagnosis of a psychotic disorder or alcohol dependence. Furthermore, with the exception of their prescribed substitute, participants were required to be free from the influence of drugs and alcohol on the days of testing.

Given the relatively high levels of depression and anxiety in opiate using populations (e.g. Regier et al., 1990; Regier, Rae, Narrow, Kaelber & Schatzberg, 1998), it was originally intended to recruit all control participants from a local NHS Improving Access to Psychological Therapies (IAPT) service, so that such symptomatology was similar between the two groups. However, it was necessary to broaden the range of individuals in the control group to include healthy control participants. This was in order to address the gender imbalance of patients comprising substance misuse (majority male) and IAPT (majority female) services so that our two groups were matched in terms of gender, and also because time constraints on the research meant that recruiting a sufficient number of male participants from the IAPT service would not have been possible. The final control group sample consisted of 10 participants recruited from IAPT, and 11 healthy control participants.

All participants in the control group were required to have normal or corrected-to-normal vision. IAPT participants were recruited via poster

advertisements, or from a database of the service's patients who were interested in research (this database was maintained by the IAPT service). Healthy control participants were recruited via UCL Psychology Sona System, an online service which displays study advertisements and facilitates the recruitment of members of the local community for research. Exclusion criteria for the control group were current illicit substance use, alcohol dependence or psychotic disorder, and a history of substance abuse or dependence, or alcohol dependence.

Prior to participation, all participants were required to read the relevant Participant Information Sheet (see Appendices C, D and E for the Participant Information Sheets for patient and control group participants), and written, informed consent was also obtained from all participants (see Appendices F, G and H for copies of the consent forms for the patient and control groups). Participants were compensated for their time; due to differences in time commitment from participants in each group (see section *2.5*, below), participants in the patient and control groups were reimbursed £20 and £10, respectively. Ethical approval for this study was obtained from the NHS National Research Ethics Service Committee South East Coast – Surrey (reference number 12/LO/1075; see Appendix I), and from UCL Division of Psychology and Language Sciences Ethics Committee (reference number CEHP/2013/503; see Appendix J).

2.2 Overview of experimental design

A mixed experimental design was employed. Between subjects factors were participant group (patient or control group) and attentional training group (ABM-as or ABM-n). Dependent variables in the study were AB, subjective craving and substance use. With the exception of frequency of substance use, all dependent

variables were measured at four time points (before ABM, 30 minutes following ABM, and at one-week and one-month follow-up). For most analyses, time was therefore the primary within subjects factor.

2.3 Questionnaire measures

2.3.1 Depression and anxiety

Baseline levels of depressive and anxious symptomatology were assessed using the Patient Health Questionnaire-9 (PHQ-9, range of possible scores from 0-27; Kroenke, Spitzer & Williams, 2001) and Generalized Anxiety Disorder-7 (GAD-7, range of possible scores from 0-21; Spitzer, Kroenke, Williams & Löwe, 2006), which are both routine outcome measures used across IAPT services in England. Assessment of depressive symptoms was further supplemented by the use of the Beck Depression Inventory-II (BDI-II, range of possible scores from 0-63; Beck, Steer & Brown, 1996). All three questionnaires are self-report measures assessing symptomatology occurring in the past two weeks, with higher scores representing greater levels of symptomatology.

2.3.2 Impulsivity

Trait impulsivity was assessed using the Barratt Impulsiveness Scale-11 (BIS-11; Patton, Stanford & Barratt, 1995; see Appendix K), which is a 30-item, self-report questionnaire with a possible range of scores from 30-120, with higher scores indicating greater levels of impulsivity.

2.3.3 Substance use

A 28-day substance use history was taken by means of interview. Participants were asked the following:

1. Which substances they used (including alcohol and tobacco; control group participants were excluded if they currently used substances other than alcohol or tobacco).
2. The amount they typically used on any given occasion (including the approximate cost).
3. When they last used each of these substances.
4. To estimate their usage over the previous week.
5. To work backwards and to estimate their usage over the three weeks prior to their usage in the previous week.

2.3.4 Subjective craving

Subjective craving was assessed by a three-item Visual Analogue Scale (VAS; see Appendix L). The items were: “I would like to use drugs,” “I want to use drugs,” and “I have an urge to use drugs”, each with “Not at all” and “Extremely” as their anchors. Participants were instructed to draw a vertical line that bisected the 10 centimetre horizontal scale to reflect how they felt at that particular moment in time. Low scores on this scale reflected low craving.

2.4 Attentional bias tasks

The specifications of all AB tasks are described in detail below. For reference, a summary of the tasks including which stimuli are used in each, number of trials etc. is available in Table 1.

2.4.1 Stimuli

The stimuli used were 44 picture pairs. Forty pairs – each matched for visual complexity and composition – contained one opiate-related image and one non-opiate related (neutral) image; the remaining four pairs contained neutral images only. The 40 opiate-neutral pairs were divided into five sets of eight (Sets 1-5), which were used at different stages of AB assessment and ABM. While many characteristics of the AB tasks were counterbalanced, the stimuli were not i.e. the stimuli used in each task (as described below and in Table 1) applied to all participants in the study. Examples of image pairs can be found in *Figure 1*.

Table 1
Summary of AB task specifications

Task	**% trials probe replaces neutral image**	**Stimuli used (number of presentations of each pair)**	**Total number of trials**
AB-0	50	Set 1 (8) 2 neutral pairs (8)	80 (64 critical, 16 neutral)
ABM-as	100	Sets 1-4 (16)	512 critical
ABM-n	50	Sets 1-4 (16)	512 critical
AB-1, AB-2, AB-3	50	Set 1 and 5 (8) 4 neutral pairs (8)	160[a] (128 critical, 32 neutral)

[a] Given the use of Set 1 and Set 5, 50% of critical and neutral trials assessed familiar stimuli (Set 1 and two neutral pairs from AB-0) and 50% assessed novel stimuli (Set 5 and two previously unseen neutral pairs).

2.4.2 Assessment of attentional bias

Assessment of AB took place on four separate occasions during the study: immediately before ABM (on Day 1), 30 minutes after ABM (on Day 1), and at one-week (Day 2) and one-month (Day 3) follow-up (see section *2.5*, below for an explanation of terminology). Assessment of AB was achieved using a standard visual probe task.

Figure 1: Examples of opiate-neutral (top two rows) and neutral-neutral (bottom row) picture pair stimuli used in the visual probe tasks.

The format of a single trial of the visual probe task is displayed in *Figure 2*. Each trial began with a fixation point (displayed for 500ms). A pair of images then appeared: one image to the left of the fixation point, the other to the right. Images appeared for either a short (200ms) or long (500ms) duration assessing automatic orienting, and controlled processing of attention, respectively. Image pairs were then

replaced by a probe – either an arrow pointing upwards or downwards – which was in the location of either the neutral or substance-related image, and remained on screen until a response was recorded. For tasks assessing AB, the probes replaced the opiate-related and neutral images equally often. The position of the opiate-related image, probe location, and stimulus duration were all counterbalanced, and an equal number of each probe type was presented. Participants were required to respond by indicating the direction of the arrow by pressing one of two response keys on a keyboard ('k' for upwards, 'm' for downwards) as quickly and accurately as possible. The inter-trial interval was a randomly determined duration between 250-500ms.

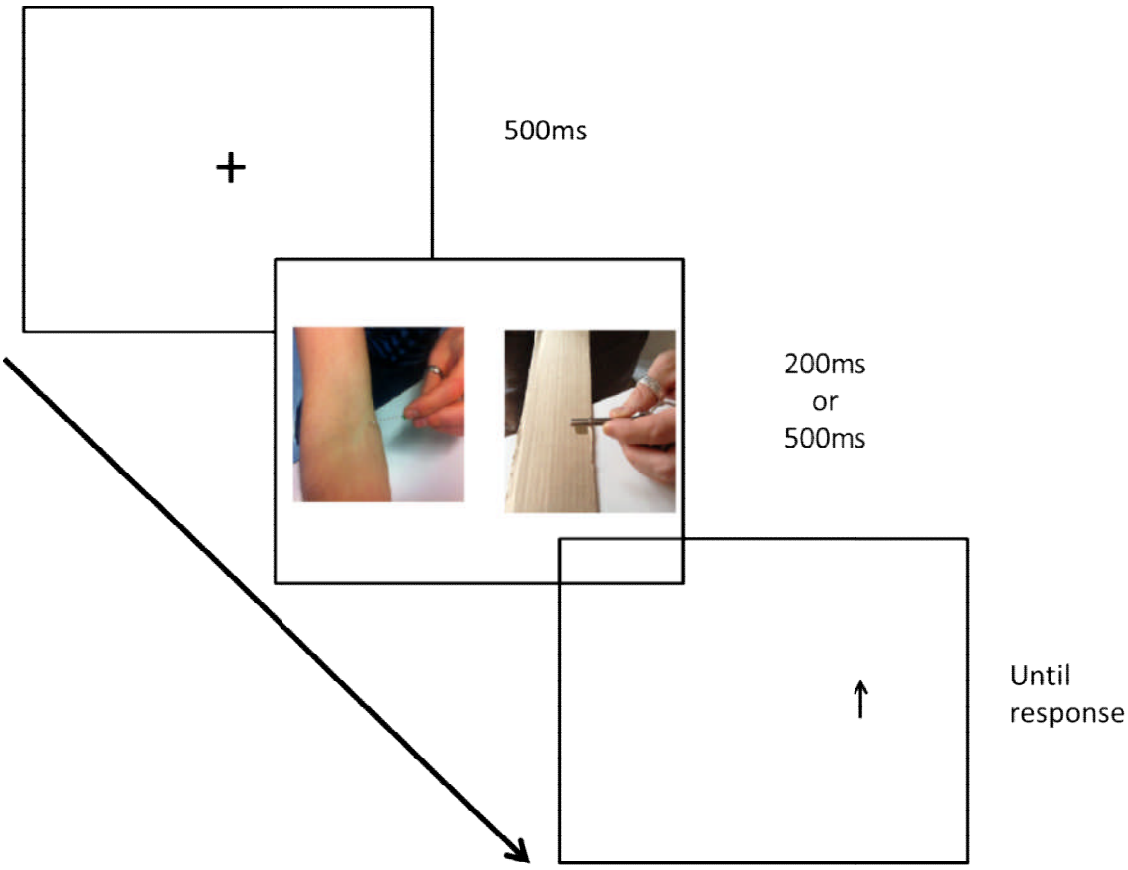

Figure 2: A visual representation of a single trial of the modified visual probe task.

2.4.2.1 Baseline assessment of attentional bias

Baseline assessment of AB (AB-0) took place on Day 1. The stimuli for this task consisted of Set 1 of the opiate-neutral pairs, plus two neutral-neutral pairs. Trials were displayed in a single block, with each pair presented eight times, producing 64 critical trials and 16 neutral trials (80 trials in total). Trials were displayed in a new random order for each participant.

2.4.2.2 Follow-up assessment of attentional bias

Follow-up assessment of AB took place after 30 minutes of ABM on Day1 (AB-1), and again on Day 2 (AB-2) and Day 3 (AB-3). Stimuli from Sets 1 and 5 were used, together with all four neutral-neutral image pairs, thus allowing the assessment of the effects of ABM on both familiar (Set 1 and two neutral pairs from AB-0) and novel (Set 5 and two unseen neutral pairs) stimuli. Each pair was presented eight times, giving 128 critical (64 familiar, and 64 novel) and 32 neutral (16 familiar, 16 novel) trials. Stimuli were presented in a single block and displayed in a new random order for each participant.

2.4.3 Attentional bias modification

ABM took place on Day 1, immediately following the completion of AB-0. Stimuli consisted of Sets 1-4 of the opiate-neutral pairs. No neutral-neutral pairs were used. Each pair was presented 16 times, producing 512 critical trials. Stimuli were presented in two blocks of 256 trials each, with participants given a short break between blocks. For participants randomised to the ABM-as group, probes replaced neutral images on 100% of trials. For participants randomised to the ABM-n group, the probe was located behind neutral images on 50% of trials, and was

counterbalanced in the same manner as the assessment of AB tasks (see section *2.4.2*, above).

2.4.4 Contingency awareness

Participants' awareness of experimental contingencies was assessed in two ways. First, participants were asked for their ideas about the purpose and aim of the study. Second, they were asked specifically whether or not they detected any patterns in the ABM task with respect to the probe location. Participants were deemed aware of the experimental contingency if either they correctly described the aim of the study or the pattern in probe location.

2.5 Procedure

An overview of the study procedure can be found in *Figure 3*. The study comprised three separate testing sessions. The first and second sessions (Days 1 and 2) took place exactly 7 days apart, and the third session (Day 3) three weeks later. Given that our control participants should not exhibit an AB towards substance-related stimuli and were not substance users, they were only required to attend Day 1 of testing. Day 1 took approximately 90 minutes to complete. Days 2 and 3 took approximately 15 and 20 minutes, respectively.

On Day 1, participants were screened by semi-structured interview for their eligibility to participate based on the criteria outlined in section *2.1*, above. Eligible participants who consented to participate were then randomly assigned to either the ABM-as or ABM-n training condition, and all participants completed baseline measures (PHQ-9, GAD-7, BDI-II, 28-day substance use history, BIS-11, VAS).

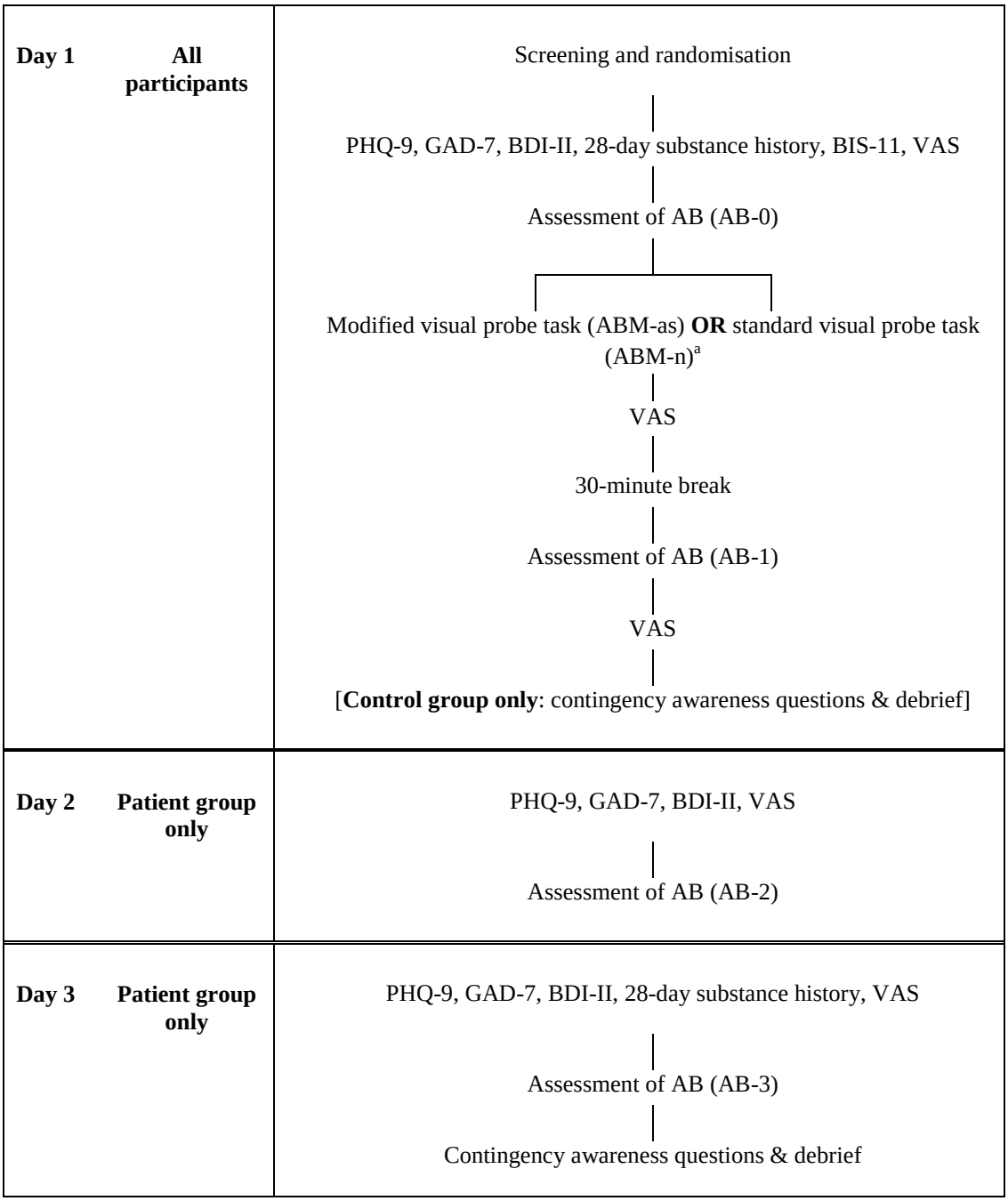

Figure 3: Overview of the experimental procedure

[a] Participants randomised to the 'avoid-substance' group completed ABM-as, whereas participants randomised to the 'neutral' group completed ABM-n.

Participants next completed AB-0, followed immediately by ABM-as or ABM-n, dependent on randomisation.

Following this, participants had a break of approximately 30 minutes. During this time they completed two unrelated tasks pertaining to a separate study (see

Wellington, 2013). AB-1 and a VAS were then administered again to re-assess AB and subjective craving, respectively.

Control participants' awareness of the experimental contingencies was assessed at the end of this testing session, and they were then debriefed and paid for their participation.

Only participants in the patient group attended Day 2 and Day 3. On these days, AB-2 and AB-3 was administered, respectively, as was the PHQ-9, GAD-7, BDI-II and VAS. A further 28-day substance use history was also taken on Day 3. At the end of Day 3, participants' awareness of experimental contingencies was assessed, participants were paid for their time and a full debrief was provided.

2.6 Data analysis

2.6.1 Attrition

Of the 23 participants in the patient group, only data from one participant were missing at one-week follow-up due to their non-attendance for testing. Full data were available from the remaining 22 participants (96% overall retention). Full data were available from all participants in the control group.

In addition, due to an administration error, craving data from one participant in the patient group assigned to ABM-n were unavailable following the 30-minute delay on Day 1 of testing.

2.6.2 Preparation of data

Checks of normality of all the data revealed that all variables were normally distributed, and there were no significant outliers (≥3 *SD*s) on key variables that warranted removal. With respect to the visual probe data, any trials where a response

error was made were excluded. Furthermore, to eliminate outliers, any trials where reaction time (RT) was less than 200ms (implausibly fast), or greater than 2000ms (likely reflecting lapses in concentration) were also excluded (c.f. Schoenmakers et al., 2007; Schoenmakers et al., 2010). All trials where neutral-neutral stimulus pairs were presented were removed for the purpose of analysis. Within opiate-neutral stimulus pairs, *attentional bias scores* were calculated by subtracting RTs to probes that replaced opiate-related stimuli from RTs to probes that replaced neutral stimuli. A positive AB score therefore indicated AB towards opiate-related stimuli. Given that RT data were normally distributed, mean RTs were used in analyses pertaining to AB tasks (c.f. Attwood et al., 2008; Field & Eastwood, 2005; Field et al., 2007; Field et al., 2009). Repeating these analyses using median data did not significantly change the results reported below.

3.0 Results

3.1 Participant characteristics

Table 2 displays summary demographic and baseline data for the participants in each group. Groups were compared on each variable using one-way ANOVAs, and *post-hoc* Bonferroni adjusted comparisons were conducted across all groups to identify significant group differences.

At baseline, there were significant differences in years of education [$F(3, 40) = 6.68$, $p = .001$], VAS 'like' [$F(3, 40) = 4.83$, $p = .006$], VAS 'want' [$F(3, 40) = 5.26$, $p = .004$], VAS 'urge' [$F(3, 40) = 6.09$, $p = .002$], BDI-II [$F(3, 40) = 4.56$, $p = .008$], and PHQ-9 [$F(3, 40) = 5.52$, $p = .003$]. *Post-hoc* analyses revealed that control participants allocated to ABM-n had significantly more years of education than both patient participants allocated to ABM-as ($p = .001$) and to ABM-n ($p = .014$), VAS

'like', VAS 'want' and VAS 'urge' was significantly greater in the patient participants allocated to ABM-n than both control participants allocated to ABM-as (like: $p = .015$; want: $p = .006$; urge: $p = .003$) and ABM-n (like: $p = .019$; want: $p = .022$; urge: $p = .006$). Further, the difference in BDI-II was driven by patient participants allocated to ABM-as scoring significantly higher than control participants allocated to ABM-n ($p = .040$), and the difference in PHQ-9 was driven by patient participants allocated to ABM-n scoring higher than control participants allocated to ABM-n ($p = .004$).

Table 2
Mean (SD) of demographic and baseline variables for each group

	Patient group		**Control group**		
	ABM-as (n=11)	ABM-n (n=12)	ABM-as (n=11)	ABM-n (n=10)	p[a]
Age	43.91 (6.77)	45.17 (8.89)	41.00 (8.53)	38 (6.68)	
Gender (M:F)	10:1	10: 2	8:3	7:3	
Years of education	11.91 (1.64)	13.33 (2.81)	14.00 (4.02)	17.30 (2.32)	**
Methadone dose	62.75 (25.78)	60.56 (36.70)	-	-	
Buprenorphine dose	9.33 (2.31)	7.33 (7.57)	-	-	
Opiate use[b]	4	8	-	-	
BDI-II	22.7 (13.9)	21.8 (10.3)	10.6 (13.1)	8.4 (7.0)	**
PHQ-9	10.7 (6.3)	13.3 (6.2)	6.4 (7.5)	3.6 (3.7)	**
GAD-7	9.1 (7.4)	7.3 (6.1)	4.6 (5.9)	6.3 (3.9)	
BIS	66.9 (11.4)	72.9 (19.9)	58.6 (13.5)	59.0 (8.3)	
VAS 'like'	2.1 (2.3)	3.4 (3.5)	0.4 (0.7)	0.4 (0.7)	**
VAS 'want'	1.8 (2.0)	3.1 (3.1)	0.1 (0.2)	0.5 (1.0)	**
VAS 'urge'	1.3 (1.7)	3.3 (3.4)	0.1 (0.2)	0.3 (0.7)	**

Note: Mean total scores are displayed for the PHQ-9, BDI-II, GAD-7 and BIS-11 measures; VAS 'like': the extent to which a participant 'would like to use drugs'; VAS 'want': the extent to which a participant 'wants to use drugs'; VAS 'urge': the extent to which a participant 'has an urge to use drugs'. See section *2.3* for details of these measures and their interpretation.
[a] *p<.05, **p<.01, ***p<.001.
[b] Denotes the number of participants that were using illicit opiates in addition to their prescribed substitute.

3.2 AB at baseline

Following preparation of the data obtained from AB-0 (see section *2.6.2*), a total of 94 (3.4%) trials were excluded due to incorrect responses, and a further 56 (2%) due to reaction times being beyond the pre-specified limits.

Patient participants did not differ significantly from control participants on stimuli displayed for 200ms [$t(42) = -0.11$, $p = .912$], but there was a trend at 500ms [$t(42) = -1.92$, $p = .066$] where contrary to prediction, patient participants ($M = -24.53$, $SD = 83.34$) showed a slight bias *away* from substance-related stimuli relative to control participants ($M = 11.16$, $SD = 30.91$).

3.3 Effects of ABM on AB

3.3.1 Immediate effects for all participants

Only AB scores for familiar stimuli (50% of critical trials) were used from AB-1. In addition to trials removed from AB-0, 62 (2.3%) trials due to error and a further 9 (0.3%) due to reaction time were removed from the data available from AB-1.

AB scores were analysed using a mixed-design 4x2x2 ANOVA, with a between-subjects factor of group (4 levels: patient ABM-as, patient ABM-n, control ABM-as, control ABM-n), and two within subjects factors of duration of stimulus presentation (2 levels: 200ms, 500ms) and time (2 levels: AB-0, AB-1).

The predicted interaction between group and time was non-significant [$F(3, 40) = 0.82$, $p = .491$, $\eta_p^2 = .058$]. Furthermore, there were no other significant main effects or interactions.

3.3.2 Effects over time for the patient group

Table 3 displays the total number and percentage of trials excluded from each AB task for the opiate group participants; overall, these were low (~2%).

AB scores were analysed using a mixed-design 2x2x4 ANOVA, with a between-subjects factor of ABM condition (2 levels: ABM-as, ABM-n), and two within subjects factors of duration of stimulus presentation (2 levels: 200ms, 500ms) and time (4 levels: AB-0, AB-1, AB-2, AB-3).

The predicted two-way interaction between ABM condition and time was non-significant [$F(1.708, 34.168) = 0.34$, $p = .683$, $\eta_p^2 = .017$; Greenhouse-Geisser adjusted]. In addition, there were no other significant main effects or interactions.

Table 3
Total number and percentage of trials excluded due to incorrect response or reaction times beyond the pre-specified limits

	Errors		**Reaction time beyond pre-specified limits**	
	n trials removed	% trials removed	*n* trials removed	% trials removed
AB-0	55	3.7	49	3.3
AB-1	40	2.7	2	0.1
AB-2	51	3.6	3	0.2
AB-3	47	3.2	0	0

Note: data displayed for AB-1, AB-2 and AB-3 represent data for trials with familiar stimuli only.

3.4 Effects of ABM on craving for patient group on Day 1

Craving data for VAS 'like', 'want' and 'urge' were analysed separately using a mixed-design 2x3 ANOVA, with a between-subjects factor of ABM condition (2 levels: ABM-as, ABM-n), and a within-subjects factor of time (3 levels: pre-ABM, post-ABM, after 30-minute delay).

The predicted interaction between ABM condition and time was non-significant for any VAS subscale (all *p*s > .400), as were all other main effects and interactions.

3.5 Other main analyses

Given there were no significant effects of ABM on AB or craving measures, secondary analyses on generalisation of ABM to novel stimuli, and cravings and frequency of substance use at follow-up were not conducted. In addition, only one control participant allocated to ABM-as correctly identified the contingency in the ABM task and so no analyses on the role of contingency awareness were conducted.

3.6 Secondary analysis: the role of treatment adherence

Given the tendency for an AB away from opiate-related stimuli in patient participants relative to control participants, which was found previously to be found associated with treatment variables (Constantinou et al., 2010), the role of adherence to treatment was explored. Treatment adherence was determined by participants' self-reported 28-day substance use history.

At baseline, 12 patient participants reported using illicit opiates on top of their prescribed substitute, while 11 reported not using on top. Table 4 displays baseline data for participants using on top and not using on top alongside that for all control participants.

Groups were compared on each variable in Table 4 using one-way ANOVAs, and *post-hoc* Bonferroni adjusted comparisons were conducted across all groups to identify significant group differences. There were significant differences in BDI-II [$F(2, 41) = 7.01$, $p = .002$], PHQ-9 [$F(2, 41) = 8.59$, $p = .001$], and BIS-11 scores

[$F(2, 41) = 5.59$, $p = .007$]. For the BIS-11 and PHQ-9 scores, participants using on top had significantly greater scores on each measure than control participants (BIS-11: $p = .005$; PHQ-9: $p = .001$). For the BDI-II score, both participants using on top ($p = .005$) and not using on top ($p = .028$) had significantly higher scores than control participants.

Table 4
Clinically relevant variables at baseline for opiate dependent participants who were using on top, not using on top, and control participants.

	Patient group		**Control group**	
	Not using on top (n=11)	Using on top (n=12)	(n=21)	p[a]
Methadone dose	74.33 (44.14)[b]	54.64 (20.48)[c]	-	
BDI-II	21.1 (7.4)	23.3 (15.1)	9.6 (10.5)	**
PHQ-9	10.1 (3.6)	13.9 (7.6)	5.1 (6.0)	**
GAD-7	7.1 (6.0)	9.1 (7.3)	5.4 (5.0)	
BIS-11	64.4 (14.0)	75.3 (17.1)	58.8 (11.0)	**
VAS 'like'	1.2 (1.6)	4.2 (3.3)	0.4 (0.6)	***
VAS 'want'	1.2 (1.7)	3.7 (2.9)	0.3 (0.7)	***
VAS 'urge'	0.8 (1.47)	3.7 (3.2)	0.2 (0.5)	***

Note: Buprenorphine dose is not reported due to low numbers of participants in the non-abstinent group (n=1).
[a] *p<.05, **p<.01, ***p<.001.
[b] n=6; the 5 other participants in this group were prescribed buprenorphine
[c] n=11; the 1 other participant in this group was prescribed buprenorphine

In addition, there were significant baseline differences in VAS 'like' [$F(2, 41) = 15.53$, $p < .001$], VAS 'want' [$F(2, 41) = 13.39$, $p < .001$] and VAS 'urge' [$F(2, 41) = 14.71$, $p < .001$]. In all cases participants using on top reported significantly higher cravings than both those who did not use on top (like: $p = .001$; want: $p = .006$; urge: $p = .001$) and control participants (all subscales: $p < .001$). There was no significant difference in methadone dose between participants who did and did not use on top [$t(15) = 1.27$, $p = .222$].

Table 5 displays the number of patient participants using other illicit and licit psychoactives in the two opiate dependent sub-groups. Due to the small numbers, statistical analyses were precluded. However, inspection of Table 5 suggests a preponderance (7/12) of those using illicit opiates on top also used crack, and all of them reported using heroin and crack together. In the other sub-group, none were using crack. For other substances, the groups were similar, although of the few that were using alcohol, those that were using illicit opiates on top reported consuming larger quantities. Owing to administration error, only quantity data for one of the three benzodiazepine using participants in the using on top group were available, thus preventing comparison between groups. Finally, there was great variation in the quantities of different psychoactives used by different participants, as evidenced by the large standard deviations.

Table 5

Number of patient participants using illicit substances on top of their prescribed substitute, including mean quantity used over the past 28-days for each group.

	Not using on top (*N*=11)		**Using on top (*N*=12)**	
	n using	Mean (*SD*)	*n* using	Mean *(SD)*
Opiates (g)	-	-	12	2.48 (2.64)
Crack cocaine (g)	0	-	7	1.87 (1.73)
Cannabis (*n* joints)	2	40.5 (55.86)	4	28.25 (26.79)
Alcohol (units per week)	4	7.00 (9.42)	3	43.67 (14.15)
Benzodiazepines (mg)	5[a, b]	181.00 (220.43)	3[c, d]	532.00 (0.00)

[a] 1 participant was on a reducing prescription for diazepam
[b] Quantity used data missing for 1 participant who reported using
[c] 2 participants were on a reducing prescription for diazepam
[d] Quantity used data missing for 2 participants who reported using

Table 6 displays the mean baseline AB scores for each group. When stimulus duration was collapsed, there was a significant difference between groups on AB at baseline [$F(2, 41) = 3.67$, $p = .034$] whereby participants not using on top had a

significantly lower AB score than control participants (p = .050). The negative AB score indicates that the attention of participants not using on top was drawn *away* from opiate-related stimuli and *towards* neutral stimuli to a greater extent than control participants. In addition, there was a trend-level difference between participants who used on top and those that did not (p = .078), again with participants who did not use on top showing lower AB relative to participants who did use on top. When broken down by stimulus duration, there was a trend in the same direction for stimuli presented at 500ms [$F(2, 41) = 3.07$, p = .057], but this was non-significant at 200ms [$F(2, 41) = 1.03$, p = .366].

In terms of patient participants' use on top over time, this remained fairly stable over the course of the study, as at one month follow-up, 10 reported using on top, and 13 reported not using on top.

Table 6
Baseline attentional bias scores for patient participants who use on top, do not use on top, and control participants.

	Patient group		**Control group**	
	Not using on top (n=11)	Using on top (n=12)	(n=21)	p[a]
AB at 200ms	-31.63 (97.98)	11.68 (74.13)	-6.57 (54.28)	
AB at 500ms	-46.56 (54.88)	-4.34 (101.11)	11.16 (30.91)	
AB (collapsed)	-37.48 (52.98)	3.23 (53.35)	1.82 (26.31)	*

[a] *p<.05, **p<.01, ***p<.001.

4.0 Discussion

The results of the present study did not support the main hypotheses. Specifically, there was no immediate effect of ABM on AB in either opiate dependent or control participants, nor was there any effect of ABM on AB over a one month period in opiate dependent participants. There was also no immediate effect of ABM on subjective craving in opiate dependent participants. Consequently,

additional analyses on generalisation of ABM to novel stimuli, and on subjective cravings and frequency of substance use over a one month follow-up period were not conducted. However, these findings were in the context of the unexpected result that there was no significant difference in baseline AB between opiate dependent and control participants, which is contrary not only to the prior research indicating AB in substance users in general (see Field & Cox, 2008), but also specifically in opiate users relative to control participants (Constantinou et al., 2010; Fadardi & Ziaee, 2010; Franken et al., 2000; Lubman et al., 2000).

4.1 Possible reasons for non-significant findings

Secondary analyses conducted around treatment adherence for opiate dependent participants went some way to illuminating the possible reason for these non-significant findings. By examining the opiate dependent participants in terms of whether or not they were using illicit opiates on top of their prescribed substitute, some interesting group differences emerged. Specifically, those using illicit opiates on top scored significantly higher at baseline than control participants on depressive symptomatology and impulsivity. In addition, participants using on top had significantly greater craving for substances at baseline than *both* patient participants not using on top *and* control participants.

Clinically, the non-significant differences between participants not using on top and control participants on measures of psychopathology and craving are also very illuminating; participants not using on top in this study, although currently opiate dependent, did not differ from control participants on measures of subjective craving, impulsivity or on one of the measures of depression administered. In fact, on the basis of the data presented here, participants not using on top and control

participants were difficult to distinguish; there was only a significant difference on one measure (BDI-II score).

There were also interesting findings from these secondary analyses in relation to baseline AB. Here, participants not using on top showed a significant bias *away* from substance-related stimuli and *towards* neutral stimuli relative to control participants when data were collapsed across both 200 and 500ms stimulus durations. In addition, there was a trend level difference between the same two groups at the 500ms duration (assessing controlled processing of attention), but no difference between them at the 200ms stimulus duration (assessing automatic orienting of attention). Taken together, this is suggestive that participants not using on top were perhaps actively directing attention away from substances, whereas other participants were not doing so. Although information about use on top beyond 28 days was not gathered, this possibly accords with Constantinou et al.'s (2010) finding that ex-opiate users showed a bias away from substance-related stimuli that correlated positively with length of abstinence, and extends those findings to specify within treatment differences that may be predictive of "recovery" (i.e. ex-opiate user status). It is important to note, however, that the opiate-related stimuli used in the AB tasks consisted of heroin and its paraphernalia, but *not* of methadone or buprenorphine. This may, therefore, be another possible reason why participants not using on top did not show a bias towards the opiate-related stimuli.

The results of these secondary analyses therefore provide a possible reason for the null findings in relation to the major hypotheses. It seems that our sample of opiate dependent participants were relatively 'stable' i.e. many reported not using on top, and those who were had relatively low levels of opiate use on top of their prescription. Indeed, this stability hypothesis is supported by the remarkably high

retention rate of this group in this study (96% over one month), which, when compared to other studies of a similar nature is particularly impressive and unusual. For example, Schoenmakers and colleagues (2010), in their ABM study with alcohol dependent participants, had a retention rate of 86% over an approximately two-week period in which time the researchers had more than five separate contacts with them. Fadardi and Cox (2009), in their ABM study with heavy drinkers had even poorer retention rates for their heaviest drinking sub-group (60% after five weeks). Therefore, had a greater proportion of our opiate dependent participants been using on top, it is possible that significant results would have been found, both in terms of baseline AB relative to control participants, and in terms of the effect of ABM on AB and possibly on other variables such as subjective craving. Unfortunately, the present sample was not large enough to explore these possibilities through running analyses examining only participants using on top and control participants.

4.2 Methodological issues

An important caveat to the findings presented here is that of statistical power, particularly with respect to the secondary analyses described above; since the opiate dependent group was split for these analyses, quite low numbers of participants were entered into some analyses. *A priori* power analysis was conducted for the effect of ABM on AB, and not for the analyses reported in the secondary analysis section. Therefore, the conclusions drawn from these analyses must be treated with caution.

However, it is possible the lack of significant findings with respect to the main hypotheses was also due to low statistical power. While *a priori* power analysis suggested that the sample size here ought to have been sufficient to detect an effect, there remains the possibility that the effect size estimates used in this power

calculation were inaccurate (i.e. larger than the true effect) given the relative infancy of research in this area (see Button et al., 2013).

Some further possible contributory factors to both the lack of observed baseline difference in AB and the lack of effect of ABM (which, it would be hypothesised, should have modified AB regardless of baseline AB) lie in the specifications of the AB task itself. While the general format of the tasks were matched closely to those used in other studies, the duration of the tasks used to assess AB at baseline and for the ABM tasks were briefer than many, thus possibly preventing both the reliable assessment of AB and successful ABM. For example, the task used to assess AB at baseline here had only 64 critical trials. While this is comparable to most ABM studies (e.g. Field & Eastwood, 2005; Schoenmakers et al., 2010; Schoenmakers et al., 2007), these studies have not compared AB in substance users to non-users. In studies where such a comparison is made, the number of trials is greater. For example, both Constantinou and colleagues (2010) and Lubman and colleagues (2000) used visual probe tasks with 160 trials. In addition, the ABM task used here, comprising 512 trials, was again briefer than is commonly used. It was decided to make our ABM task briefer to avoid a very lengthy testing session, as we reasoned this may have affected participant retention and the quality of data collected amongst opiate dependent participants. We based the specification of our ABM task loosely on that of Schoenmakers et al. (2010) given that they also recruited a clinical sample. While their ABM task featured only 528 trials, it is noteworthy that they administered the task on five separate occasions, thus increasing the number of trials to 2640. Therefore, for ABM to have been successful, it may be the case that a greater number of trials were needed, either in

one lengthy session (e.g. as per Field et al., 2007, who used 960 trials), or split between multiple training sessions.

Another possible factor was the motivation of participants. Participants were not informed of the experimental contingencies, in keeping with most of the literature to date, and only one participant correctly identified the contingency. Participants therefore may not have been well motivated, although no measure of motivation was given to explicitly assess this. However, the extent to which awareness and motivation are important is unclear, as mixed findings have been reported. For instance, Field et al. (2009) found no significant effect of contingency awareness, while both Schoenmakers et al. (2010) and Fadardi and Cox (2009) explicitly informed participants of contingencies and reported positive results. However, both of these latter studies also employed multiple sessions of ABM, which may therefore have been a more important factor than awareness and motivation.

4.3 Clinical and research implications

The results of the secondary analyses on treatment adherence raise several important clinical implications. First, the data suggested high levels of depression in participants who reported using on top. Indeed, the two might be related. It may therefore be worthwhile services screening for depression in patients who are using on top, or who begin using on top after a period of not doing so.

Second, while the differences in methadone dose did not reach statistical significance, it is worth noting that there was a large difference between the mean dose in participants who reported using on top and those who reported not using on top. Specifically, those using on top had a mean dose of approximately 20mg less and with less variance in dosage. Caution in interpretation of these figures is needed

since the number of participants entered into this analysis was small, although it raises the possibility that participants using on top were receiving an inadequate dose of methadone which may have been contributing to their use on top. Indeed, there is some evidence in the literature of better outcomes with higher doses. For example, a randomised trial found that higher doses (80-100mg) were more effective in achieving abstinence from additional, illicit heroin use and in achieving complete detoxification compared to lower doses (40-50mg) (Strain, Bigelow, Liebson & Stitzer, 1999). It is worth noting that the most successful dose in this trial (80-100mg) is substantially greater than the mean dose of participants using on top in this study (~55mg). In addition, the reduced use of illicit heroin on top in individuals prescribed higher methadone doses is supported by a naturalistic study examining opiate users in treatment across eight different substance misuse clinics (Trafton, Minkel & Humphreys, 2006). Interestingly, this same study noted that effective doses were positively correlated with the presence of psychopathology, including self-reported levels of depression, leading the authors to recommend that clinical factors such as the presence of depression should also be considered when determining dosages.

Third, although no statistical comparisons were made, the data highlighted the use of crack cocaine in addition to heroin as a particular problem. In this sample, seven of the twelve participants who used illicit opiates on top of their methadone/buprenorphine used crack cocaine in conjunction with these illicit opiates, whereas no participants who were not using illicit opiates on top reported using crack. This reflects current ‘street deals’ whereby heroin and crack are sold in tandem. The data also highlighted alcohol consumption in larger quantities in those participants who used illicit opiates on top. Services should therefore be alert to

conjoint crack cocaine use and possible higher levels of alcohol consumption in patients who are using illicit opiates on top of their prescribed substitute.

In terms of future research, several important considerations emerge from the present study. First, any future ABM studies with opiate dependent individuals should consider not using on top as an exclusion criterion to increase the likelihood of ABM being useful in this group, since it is possible it is individuals who use on top that have significant AB towards substances and significantly greater subjective cravings. However, if participants who do not use on top are included in future research, a second recommendation would be to include as stimuli images of methadone and buprenorphine in AB tasks to examine whether such participants exhibit an AB towards such images.

Third, the sample size in the present study was too small to conduct several analyses of interest with regard to treatment adherence and other variables. Therefore, in addition to repeating the analyses examining this study's main hypotheses in light of treatment adherence information, future studies with larger samples may also wish to examine, for example, the association between AB and subjective craving and methadone or buprenorphine dose at baseline, and the differences in licit and illicit substance use (e.g. use of cannabis, alcohol, etc.) between patients who do and do not use illicit opiates on top.

A fourth consideration would be the number of trials used in AB tasks. For example, in ABM tasks, future research with this group should either utilise a greater number of trials in a single session, or employ multiple training sessions each of relatively briefer duration. While the use of multiple sessions may seem preferable given the positive outcomes reported elsewhere in the literature, retention of participants may then become an issue. Given the lack of significant effects found

here, in the first instance it may be sensible to attempt a single, lengthier session with multiple breaks to assess whether ABM is a fruitful avenue of research with this population. Should it produce significant effects, it may then be better justified to conduct a study examining the effect of multiple training sessions.

Finally, while the hypotheses of the present study were not supported by the data, the clinical and conceptual implications of the secondary analyses' findings are nevertheless important. For instance, it may not be useful for both clinical or research purposes to consider opiate dependent populations homogenous. Rather, patients who use on top and patients who do not may be quite separable in terms of their psychopathology and attentional functioning.

5.0 References

Algom, D., Chajut, E., & Lev, S. (2004). A rational look at the emotional Stroop phenomenon: a generic slowdown, not a Stroop effect. *Journal of Experimental Psychology: General*, *133*, 323-338.

Attwood, A. S., O'Sullivan, H., Leonards, U., Mackintosh, B., & Munafò, M. R. (2008). Attentional bias training and cue reactivity in cigarette smokers. *Addiction*, *103*, 1875-1882.

Bearre, L., Sturt, P., Bruce, G., & Jones, B. T. (2007). Heroin-related attentional bias and monthly frequency of heroin use are positively associated in attenders of a harm reduction service. *Addictive Behaviors*, *32*, 784–792.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.

Bradley, B., Field, M., Mogg, K., & DeHouwer, J. (2004). Attentional and evaluative biases for smoking cues in nicotine dependence: component processes of biases in visual orienting. *Behavioural Pharmacology*, *15*, 29-36.

Button, K. S., Ioannidis, J. P. A., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S. J., & Munafò, M. R. (2013). Power failure: why small sample size undermines the reliability of neuroscience. *Nature Reviews Neuroscience, 14*, 365-376.

Carpenter, K. M., Schreiber, E., Church, S., & McDowell, D. (2006). Drug Stroop performance: relationships with primary substance of abuse and treatment outcome in a drug-dependent outpatient sample. *Addictive Behaviors, 31*, 174-181.

Constantinou, N., Morgan, C. J. A., Battistella, S., O'Ryan, D., Davis, P., & Curran, H. V. (2010). Attentional bias, inhibitory control and acute stress in current and former opiate addicts. *Drug and Alcohol Dependence, 109*, 220-225.

Copersino, M. L., Serper, M. R., Vadhan, N., Goldberg, B. R., Richarme, D., Chou, J. C. Y., … Cancro, R. (2004). Cocaine craving and attentional bias in cocaine-dependent schizophrenic patients. *Psychiatry Research, 128*, 209-218.

Cox, W. M., Blount, J. P., & Rozak, A. M. (2000). Alcohol abusers' and nonabusers' distraction by alcohol and concern-related stimuli. *American Journal of Drug and Alcohol Abuse, 26*, 489-495.

Cox, W. M., Hogan, L. M., Kristian, M. R., & Race, J. H. (2002). Alcohol attentional bias as a predictor of alcohol abusers' treatment outcome. *Drug and Alcohol Dependence, 68*, 237-243.

Fadardi, J. S., & Cox, W. M. (2009). Reversing the sequence: reducing alcohol consumption by overcoming alcohol attentional bias. *Drug and Alcohol Dependence, 101*, 137-145.

Fadardi, J. S., & Ziaee, S. S. (2010). A comparative study of drug-related attentional bias: evidence from Iran. *Experimental and Clinical Psychopharmacology, 18*, 539-545.

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*, 175-191.

Field, M. (2005). Cannabis ‘dependence’ and attentional bias for cannabis-related words. *Behavioural Pharmacology, 16*, 473-476.

Field, M. (2006). Attentional biases in drug abuse and addiction: cognitive mechanisms, causes, consequences, and implications. In M. Munafò, & I. P. Albery (Eds.), *Cognition and Addiction* (pp. 73-99). Oxford, United Kingdom: Oxford University Press.

Field, M., & Cox, W. M. (2008). Attentional bias in addictive behaviors: A review of its development, causes, and consequences. *Drug and Alcohol Dependence, 97*, 1-20.

Field, M., Duka, T., Eastwood, B., Child, R., Santarcangelo, M., & Gayton, M. (2007). Experimental manipulation of attentional biases in heavy drinkers: do the effects generalise? *Psychopharmacology, 192*, 593-608.

Field, M., Duka, T., Tyler, E., & Schoenmakers, T. (2009). Attentional bias modification in tobacco smokers. *Nicotine & Tobacco Research, 11*, 812-822.

Field, M., & Eastwood, B. (2005). Experimental manipulation of attentional bias increases the motivation to drink alcohol. *Psychopharmacology, 183*, 350-357.

Field, M., Eastwood, B., Bradley, B. P., & Mogg, K. (2006). Selective processing of cannabis cues in regular cannabis users. *Drug and Alcohol Dependence, 85*, 75-82.

Field, M., Munafò, M. R., & Franken, I. H. A. (2009). A meta-analytic investigation of the relationship between attentional bias and subjective craving in substance abuse. *Psychological Bulletin, 135*, 589-607.

Franken, I. H. A. (2003). Drug craving and addiction: integrating psychological and neuropsychopharmacological approaches. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 27*, 563-579.

Franken, I.H.A., Kroon, L. Y., Wiers, R. W., & Jansen, A. (2000). Selective cognitive processing of drug cues in heroin dependence. *Journal of Psychopharmacology, 14*, 395–400.

Klein, A. A. (2007). Suppression-induced hyperaccessibility of thoughts in abstinent alcoholics: a preliminary investigation. *Behaviour Research and Therapy, 45*, 169-177.

Hester, R., Dixon, V., & Garavan, H. (2006). A consistent attentional bias for drug-related material in active cocaine users across word and picture versions of the emotional Stroop task. *Drug and Alcohol Dependence*, *81*, 251–257.

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ 9: validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*, 606-613.

Lubman, D. I., Peters, L. A., Mogg, K., Bradley, B. P., & Deakin, J. F. W. (2000). Attentional bias for drug cues in opiate dependence. *Psychological Medicine, 30*, 169-175.

MacLeod, C., Rutherford, E., Campbell, L., Ebsworthy, G., & Holker, L. (2002). Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *Journal of Abnormal Psychology, 111*, 107-123.

Marissen, M.A.E., Franken, I.H.A., Waters, A.J., Blanken, P., van den Brink, W., & Hendriks, V.M. (2006). Attentional bias predicts heroin relapse following treatment. *Addiction, 101*, 1306–1312.

McHugh, R. K., Murray, H. W., Hearon, B. A., Calkins, A. W., & Otto, M. W. (2010). Attentional bias and craving in smokers: the impact of a single attentional training session. *Nicotine & Tobacco Research, 12*, 1261-1264.

Mogg, K., Bradley, B. P., Field, M., & DeHouwer, J. (2003). Eye movements to smoking-related pictures in smokers: relationship between attentional biases and implicit and explicit measures of stimulus valence. *Addiction, 98,* 825-836.

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt Impulsiveness Scale. *Journal of Clinical Psychology, 51,* 768-774.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) study. *The Journal of the American Medical Association, 264,* 2511–2518.

Regier, D. A., Rae, D. S., Narrow, W. E., Kaelber, C. T., & Schatzberg, A. F (1998). Prevalence of anxiety disorders and their comorbidity with mood and addictive disorders. *The British Journal of Psychiatry, 173, Suppl. 34,* 24–28.

Ryan, F. (2002). Detected, selected, and sometimes neglected: cognitive processing of cues in addiction. *Experimental and Clinical Psychopharmacology, 10,* 67-76.

Schoenmakers, T. M., de Bruin, M., Lux, I. F. M., Goertz, A. G., Van Kerkhof, D. H. A. T., & Wiers, R. W. (2010). Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. *Drug and Alcohol Dependence, 109,* 30-36.

Schoenmakers, T., Wiers, R. W., Jones, B. T., Bruce, G., & Jansen, A. T. M. (2007). Attentional re-training decreases attentional bias in heavy drinkers without generalization. *Addiction, 102,* 399-405.

Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing Generalized Anxiety Disorder: the GAD-7. *Archives of Internal Medicine*, *166*, 1092-1097.

Stormark, K. M, Laberg, J. C., Nordby, H., & Hugdahl, K. (2000). Alcoholics' selective attention to alcohol stimuli: automated processing? *Journal of Studies on Alcohol and Drugs*, *61*, 18-23.

Strain, E. C., Bigelow, G. E., Liebson, I. A., & Stitzer, M. L. (1999). Moderate- vs high-dose methadone in the treatment of opioid dependence: a randomized trial. *The Journal of the American Medical Association*, *281*, 1000-1005.

Tiffany, S. T. (1990). A cognitive model of drug urges and drug-use behavior: role of automatic and nonautomatic processes. *Psychological Review*, *97*, 147-168.

Townshend, J. M., & Duka, T. (2001). Attentional bias associated with alcohol cues: differences between heavy and occasional social drinkers. *Psychopharmacology*, *157*, 67-74.

Trafton, J. A., Minkel, J., & Humphreys, K. (2006). Determining effective methadone doses for individual opioid-dependent patients. *PLoS Medicine*, *3*, 0380-0387.

Waters, A. J., Shiffman, S., Sayette, M. A., Paty, J. A., Gwaltney, C. J., & Balabanis, M. I. I. (2003). Attentional bias predicts outcome in smoking cessation. *Health Psychology*, *22*, 378-387.

Wellington, C. E. (2013). *Dynamic facial affect recognition in substitute prescribed opiate users*. (Unpublished clinical psychology doctoral thesis). Department of Clinical, Educational, and Health Psychology, University College London.

Wiers, R., & Stacy, A. W. (Eds.). (2006b). *Handbook of implicit cognition and addiction*. Thousand Oaks, CA: SAGE Publishers.

Wiers, R. W., Bartholow, B. D., van den Wildenberg, E., Thush, C., Engels, R. C. M. E., Sher, K. J., … Stacy, A. W. (2007). Automatic and controlled processes and the development of addictive behaviors in adolescents: a review and a model. *Pharmacology, Biochemistry and Behavior*, *86*, 263-283.

Part 3: Critical Appraisal

Critical Appraisal

The process of completing this thesis, in both practical and academic respects, has been interesting and challenging for many different reasons. This appraisal aims to review the research process as a whole, and to hopefully provide some practical guidance to researchers who are either already in, or who hope to enter into the field of this thesis. Issues such as gaining ethical approval, joint working and recruitment of clinical samples are discussed. How the experience of doing the literature review and research impacted on my understanding of attentional bias and the modification of other implicit processes will also be discussed.

Ethics Application Process

Prior to training in clinical psychology, I worked for two years as a research assistant. This gave me good experience of many aspects of the research process. However, one area I was not familiar with was ethics application to a National Health Service Research Ethics Committee (NHS REC). While I was aware that the process was longer than for internal university ethics application processes, nothing could have prepared me for just how long it took! It goes without saying, therefore, that a recommendation to others would be to start this early.

However, while the paperwork for this process was certainly laborious and repetitive, it is important to note that progress was further hindered by a mandatory internal review process within UCL, required in order for UCL to provide sponsorship for research. In practical terms, this internal procedure (relevant to all trainees applying for NHS ethics) amounted to our whole application requiring approval *twice*. We were informed that we could not book a meeting with an NHS REC until our application had been reviewed internally, which delayed our ability to

approach an NHS REC by approximately six weeks. This was certainly frustrating, but it was made more frustrating by the fact that some of the feedback given regarding the application was inaccurate, and therefore complicated completion of the form since clarification was required before proceeding. I believe this process is something that needs reconsidering. After all, given that supervisors are Principal Investigators on all NHS studies, is their sign-off on an application prior to submission to an REC not sufficient? Trainees are not afforded a great deal of time to conduct their research for their thesis owing to commitments to clinical placements; the removal of this additional process would therefore allow for a valuable few additional weeks of recruitment.

On another ethics related note, a point worthy of consideration before approaching services is the method of paying participants. A question that was regularly asked of us when discussing the research with staff in services was what form payment would take, with a discussion emerging around the ethical implications of paying substance users in cash and whether they should instead be paid in vouchers. I understand the objection, and as an example I recall some participants telling me that they only use heroin when they can afford to buy it i.e. when they are paid their benefits. It may follow, therefore, that the £20 they received from us may have gone towards funding their substance use. However, this would not be true of all participants. My personal stance on this issue straightforward: I see no ethical reason why substance users should not be paid in cash, in the same way as control participants are. They are, after all, adults with capacity and are capable of making their own decisions. Indeed, by inviting them to take part in research, we are by definition seeing them as adults with capacity. Some may not consider their decisions wise, but that is up to the individual. Whatever one decides regarding

payment, however, it would be worthwhile preparing to communicate your reasoning to services since this will certainly be required.

Shared Projects

The research project was conducted jointly with a fellow trainee clinical psychologist and this was very helpful throughout the research process. Essentially, it meant that the workload for each of us was halved, including completing forms for the ethics application, gathering of research materials and recruitment and data collection. Ensuring that each of us was available for testing on different days of the week to one another also meant that we were able to increase our range of potential participants, which was certainly a strength of the way that we worked together.

Joint working was not without its drawbacks, however, including the occasional argument when we disagreed on a certain decision that needed to be made. Sadly, this was often over relatively trivial things. Of course, this is inevitable when two people spend often long periods of time with one another when both are under a lot of stress. Fortunately, however, these occasions were few, and on the whole, joint working was a very positive experience. After all, it is nothing but entertaining when you have both spent the afternoon photographing heroin paraphernalia in your flat, only for a flatmate to come home, find needles and dirty spoons all over the kitchen, and have a look of shock and horror slowly spread across their face as they think you have converted the place into a drug den!

Issues in Recruitment

Given the time constraints of data collection, an early start was imperative. This was even truer given that we were recruiting both experimental and control groups from clinical populations.

I found the recruitment of each group to be surprising for very different reasons and, in fact, the outcome was the opposite of what I predicted prior to starting. I had expected that recruitment of opiate dependent participants would be difficult, and also that retention of this group for follow-up sessions would be challenging. On the contrary, recruitment went well with this group. While it was true that there were a sizeable number of participants who did not attend their appointment for the initial session of the research, there were still many who did attend. Furthermore, only one participant failed to attend one of the follow-up sessions; retention was otherwise seamless.

On the other hand, while I had expected recruitment of IAPT control participants to run relatively smoother, this is not what happened. We instead found that we struggled to accrue sufficient numbers, ultimately leading us to apply for ethical approval to expand our potential pool of control participants to include healthy individuals outside any treatment setting.

I think the reasons for this were varied. With respect to the opiate dependent participants, the fact that we had an on-site supervisor who was a regular collaborator on trainee research and who was very well-placed to get the study up-and-running from the beginning helped a great deal. Being a regular collaborator meant that he had a lot of research experience, particularly in terms of the practicalities of recruiting and testing participants at the service where he works. His advice and guidance were therefore extremely helpful. In fact, the whole team at the service were very welcoming and friendly, and many of the key workers were very helpful in the recruitment process by discussing the research with their patients and referring interested persons on to us as researchers.

One innovation which proved very useful was the approach that we took in terms of our contact with the opiate dependent participants. Here, we mirrored the service in that we took a more 'assertive' approach. What this meant was that we would contact patients by telephone or text message regularly to remind them of appointments. While this is very different to the way in which many services operate, it was *very* effective in terms of ensuring attendance of participants. This was evidenced by our very high retention rate (96% over one month) which is much better than reported elsewhere in the literature on research with substance using individuals.

Regarding control participants from the IAPT service, one factor that was not originally considered was that many of the service's patients are employed meaning that testing during working hours was not feasible. While we did later arrange to test during the evenings at a different location, we initially missed out on this opportunity, thus slowing our recruitment down. In addition, given that our contacts at the IAPT site were not as closely linked to the research as at the substance misuse service, it meant we were able to spend less time on site making ourselves familiar to both staff and potential participants, and therefore were not able to do as much 'promotion' of our study. In addition, we had hoped that expanding our recruitment methods by gaining access to the IAPT service's database of patients interested research would lead to swifter recruitment. Again, however, I think reality did not meet our expectations; we had perhaps anticipated many patients existing on this database, when in fact we were initially passed the details for just seven people. Taken together, these factors ultimately led to us widening our control sample to include healthy participants. Again, offering testing sessions on evenings and weekends was helpful, as these were the most opted-for of all of the appointments.

Sample Size and Statistical Power

As discussed in Volume 1 Part 2 of this thesis, one possible significant contributory factor to non-significant findings in the study was related to whether or not opiate dependent participants were using illicit opiates on top of their prescribed substitute medication. However, another point worthy of discussion is that of statistical power. Although this was also discussed in Volume 1 Part 2, I think it is worthy of an expanded discussion here. According to *a priori* calculations, the study presented in this thesis was sufficiently powered to detect an effect. However, while that is true, one cannot help but question whether or not that is indeed the case given that the total sample size was still just 44, and less for some analyses. After all, the two prior attentional bias modification (ABM) studies that offered effect size estimates quoted Cohen's *d* as 0.87 and 1.27. These figures are large and very large, respectively (Cohen, 1992) and therefore for me seem rather unlikely; perhaps the true effect size is very different, but given that there have been so few studies to date it is possible that these estimates are inaccurate. Indeed, they are very different between the two studies themselves.

A recent study led to my questioning of this. Button and colleagues (2013) reviewed recent meta-analyses in neuroscience, and then using the estimated true effect size given in these meta-analyses, retrospectively calculated the power of the individual studies to detect these effects. What the authors found was startling: a median statistical power of 21%. Granted, ABM research is not neuroscience and the findings cannot be assumed to be true of other fields. However, there are more general conceptual issues raised by the paper that apply to all research. For example, the study highlighted how smaller studies tend to over-estimate the effect size of significant results. Since initial studies in an area, often for funding reasons, tend to

be small, it is therefore likely that an over-estimation of effect size occurs. A consequence of this is that replication studies, which base their power analysis on these effect size estimates, are therefore also likely to be underpowered. To complicate the issue further, Button and colleagues highlight how low power not only increases the risk of Type II errors, but also reduces the likelihood that a statistically significant result reflects a true effect.

The same study also highlights the fact that low power, and therefore a low-powered study, is closely associated with another bias that further complicates the picture: the 'vibration of effects'. This is a mathematical phenomenon in low-powered studies, which gives rise to a large range of effect size estimates between different studies. This may therefore explain the large discrepancy in effect size estimates provided by previous ABM studies (see above).

Taken together, in an ideal world, any initial or early studies should aim to have large sample sizes to increase power and obtain more accurate effect size estimates for any significant findings. Provided replication studies then use formal power calculations to determine sample size, this would facilitate effect size estimates converging on the true effect size sooner rather than later. Of course, while very important, practically this is very challenging.

How Conducting the Research Modified My Understanding of ABM

I found the process of conducting both the literature review and the research project a very informative experience, and it brought to light several things of which I was not previously aware in relation to modification of attentional bias and other implicit processes.

The Relative Success of Intervention across Different Disorders

I came into this research with prior experience of working in ABM as a research assistant, although this experience was with participants with mood disorders as opposed to substance misuse problems. The study that I was involved with drew on research conducted with people with anxiety disorders. One of the revealing and surprising things this thesis highlighted was the seemingly different levels of success of ABM between people with mood/anxiety disorders and substance users. For example, there are some very promising results regarding the utility of ABM in anxiety disordered individuals, with individuals receiving ABM in addition to usual treatment having better clinical outcomes relative to individuals in control groups (see MacLeod, 2012, for a review). In substance users, however, this does not appear to be as clear a finding. Specifically, the literature review highlighted that while modifying implicit processes away from substance-related stimuli is potentially helpful for substance using individuals, it seems from the evidence to date that it is actually easier to create biases *towards* such stimuli, and ultimately influence behaviour in a negative way. This was a surprising finding, but one that was commonplace in control groups in different studies.

It is important to note, however, that research into ABM for substance use is in its infancy relative to that of anxiety disorders. In time, and with refinement of the methodology, the results may become comparable. However, this may not be the case, and if so, exploration of the reasons would be very interesting. For example, one might hypothesise that attentional bias in substance users may be more biologically driven (if, as it is argued, it is a consequence of a process such as incentive sensitisation; see Robinson & Berridge, 1993), making its modification more difficult.

Ways Forward with Intervention Research: Public Health Initiatives?

This raises interesting questions about the way to proceed in research of this type, not only for opiate users, but for substance users more generally. It is certainly worthwhile continuing to explore whether multiple sessions of ABM are helpful in clinical groups of substance users, as it may indeed prove to be a useful adjunct to regular treatments. However, it seems another way to address the problem would be to take a public health approach, and rather than attempt to modify attentional bias in substance users on an individual level one could take broader steps to remove the environmental cues that grab attention.

Indeed, this is an approach that has been adopted in Australia in an effort to reduce the rates of tobacco smoking. As of December 2012, all tobacco products sold in Australia must be sold in plain packaging (The Parliament of the Commonwealth of Australia, 2011). The evidence upon which this measure was based suggests that plain packaging could reduce the number of young people taking up smoking (see Quit Victoria, 2011). To date, data are not available on the relative success of the measure due to the short time it has been in force, but such data will undoubtedly be eagerly anticipated by other countries also considering the move. The British government has also recently considered this for England, holding a consultation on the matter in 2012. Although, rather disappointingly in my opinion, they recently decided that further progress on the matter will be delayed. In any case, should England and other nations eventually decide to take a similar approach, there will almost certainly be a significant barrier to the process, namely the tobacco industry. This industry remains very influential and powerful, and thus costly legal battles are likely to ensue following the passing of any such law, as indeed is the case in Australia.

More broadly, while it is certainly a worthwhile enterprise to target tobacco smoking with such interventions, one could make an argument that alcohol should also be targeted in a similar manner. After all, there is some evidence from expert opinion to suggest that alcohol is the most harmful substance in the UK above heroin and crack cocaine (Nutt, King & Phillips, 2010). It is true that minimum pricing of alcohol has been considered recently in England, although like plain packaging for tobacco, the plans have been delayed. Similar to the Australian government over tobacco packaging, other countries that have taken steps to implement a minimum price for alcohol (e.g. Scotland) have faced lengthy and costly legal battles against industry. It is possible political change to overrule competing demands of the substance-producing industry as well as attitudinal change at a societal/cultural level are required before these measures can be passed without such great opposition and consequent great expense to the taxpayer.

References

Button, K. S., Ioannidis, J. P. A., Mokrysz, C., Nosek, B. A., Flint, J., Robinson, E. S. J., & Munafò, M. R. (2013). Power failure: why small sample size undermines the reliability of neuroscience. *Nature Reviews Neuroscience, 14*, 365-376.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*, 155-159.

MacLeod, C. (2012). Cognitive bias modification procedures in the management of mental disorders. *Current Opinion in Psychiatry, 25*, 114-120.

Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: a multicriteria decision analysis. *The Lancet, 376*, 1558-1565.

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Research Reviews, 18*, 247-291.

The Parliament of the Commonwealth of Australia. (2011). *Tobacco Plain Packaging Bill, 2011*. Retrieved May 2013, from http://parlinfo.aph.gov.au/parlInfo/download/legislation/bills/r4613_aspassed/toc_pdf/11136b01.pdf;fileType=application%2Fpdf

Quit Victoria, Cancer Council Victoria. (2011). *Plain packaging of tobacco products: a review of the evidence*. Retrieved May 2013, from http://www.cancer.org.au/content/pdf/CancerControlPolicy/PositionStatements/TCUCCVBkgrndResrchPlainPak270511ReEnd_FINAL_May27.pdf

Appendices

Appendix A

Search terms used for literature search conducted on 31 August 2012:

Example of a search for the PsycInfo database

1	Attentional Bias/	429	Advanced	Display More ≫
2	attention* bias.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1583	Advanced	Display More ≫
3	implicit cogniti*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	325	Advanced	Display More ≫
4	implicit association test.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1441	Advanced	Display More ≫
5	(attentio* adj2 modification).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	99	Advanced	Display More ≫
6	evaluative conditioning.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	267	Advanced	Display More ≫
7	approach avoidance.mp. or exp Approach Avoidance/	1197	Advanced	Display More ≫
8	implicit association*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1605	Advanced	Display More ≫
9	(implicit adj2 associatio*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1684	Advanced	Display More ≫
10	implicit attitude*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	594	Advanced	Display More ≫
11	memory bias.mp.	398	Advanced	Display More ≫
12	action tendenc*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	310	Advanced	Display More ≫
13	cognitive bias modification.mp.	55	Advanced	Display More ≫
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	5881	Advanced	Display More ≫
15	drug usage.mp. or exp Drug Usage/	121691	Advanced	Display More ≫
16	drug abuse.mp. or exp Drug Abuse/	86069	Advanced	Display More ≫
17	drug addiction.mp. or exp Drug Addiction/	12864	Advanced	Display More ≫
18	exp Drug Dependency/	19832	Advanced	Display More ≫
19	drug dependenc*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	11358	Advanced	Display More ≫
20	alcohol dependenc*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	6920	Advanced	Display More ≫
21	exp alcohol drinking patterns/ or exp alcohol abuse/	49481	Advanced	Display More ≫
22	alcohol abuse.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	17829	Advanced	Display More ≫

23	alcohol drinking patterns.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	16249	Advanced	Display More ≫
24	problem drinking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1815	Advanced	Display More ≫
25	tobacco smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	20561	Advanced	Display More ≫
26	smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	33069	Advanced	Display More ≫
27	cigarette smoking.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	5180	Advanced	Display More ≫
28	cannabis us*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	2180	Advanced	Display More ≫
29	heroin us*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1621	Advanced	Display More ≫
30	substance us*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	20051	Advanced	Display More ≫
31	substance abuse.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	25149	Advanced	Display More ≫
32	substance dependenc*.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1811	Advanced	Display More ≫
33	substance addiction.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	175	Advanced	Display More ≫
34	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	155924	Advanced	Display More ≫
35	14 and 34	447	Advanced	Display More ≫
36	**limit 35 to ("0110 peer-reviewed journal" and english and human)**	**340**	**Advanced**	Display

Appendix B

Contribution of individual persons to Volume 1, Part 2 of this thesis

Appendix B

The major research component of this thesis was a joint study conducted by myself and a fellow Trainee Clinical Psychologist, Clare Wellington.

Workload related to our ethics application was shared equally. With the support of our supervisor, we each independently designed the particular aspects of our studies. Therefore, while the participants in each of our studies were the same, we each had separate experimental tasks and hypotheses.

Data recruitment began in December 2012. Between this time and March 2013, Clare and I shared equal responsibility for the recruitment and testing of participants. From March 2013 until the study's completion, we had additional assistance in data collection from Claire Mokrysz, PhD student in mental health, University College London.

Data entry was shared by Clare Wellington and I, although data analysis was conducted independently. Claire Mokrysz did not provide support in data entry or data analysis.

Appendix C

Participant Information Sheet (patient group)

Camden and Islington NHS
NHS Foundation Trust

UCL

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London, WC1E 6BT

Participant Information Sheet
Methadone- or Subutex-Maintained Participants

Study Title: Attention and Emotional Processes in Methadone- or Subutex-Maintained Opiate Users and Non-Users

Researchers: Matthew Charles (Trainee Clinical Psychologist), Clare Wellington (Trainee Clinical Psychologist) & Claire Mokrysz (PhD Student)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?

To understand how attention and emotions are involved in people's use of opiates like heroin. Research suggests that these processes may be important in why people become dependent on drugs, so we are looking at differences in attention and emotion between people who use opiates and people who don't.

Why have I been chosen?

We have asked you to take part because you are currently receiving treatment for opiate use.

Do I have to take part?

No, you do not have to take part in the study if you not wish to. If you are thinking of taking part you can keep a copy of this Information Sheet and you can contact us for more information if you wish. If you do decide to take part you can withdraw at any time without having to give a reason. Any decision you make will not affect your usual clinical care in any way.

What will happen if I take part?

We will arrange three meetings with you at the place where you receive your usual treatment.

The first meeting will take about 1.5 hours. During this meeting you will have another chance to ask any questions you may have about the study. We will ask you some questions about your drug use and you will be asked to complete a series of computer tasks and questionnaires.

The second meeting will be exactly 1 week later. This meeting will take no more than 30 minutes of your time and will involve completing some computer tasks and questionnaires.

The third meeting will be about 3 weeks later. Again, this will take no more than 30 minutes and you will be asked to do the same questionnaires and computer tasks as in the second meeting. After that, we will give you £20 to compensate you for your time in taking part.

What will happen to my information?

All information collected about you during the study is strictly confidential and will be coded by number.

Camden and Islington NHS
NHS Foundation Trust

UCL

Your name will not appear on any of the questionnaires you complete.

The only exception to this is if, during the course of the study, you disclose that you intend to harm yourself or other people. If this happens, we might speak to members of staff involved in your care to ensure that support is provided for you. Wherever it is possible, we would speak to you *first* to get your permission before speaking to anyone else.

What are the advantages and disadvantages of taking part?
We do not think that taking part will cause you distress. Some of the computer tasks you complete will involve looking at pictures of drugs and faces showing different emotions. There is a small chance you may experience a change in cravings or mood, but this would be temporary. Similar research that has been done in the past has never reported negative effects on those taking part. If in the unlikely event you do become distressed, there will be a member of clinical staff on hand that you can speak to. We hope that the information we collect from this study will improve our understanding of how people become and remain addicted to drugs. Through this, it is hoped this study will help to improve drug treatment services.

What should I do if I have a complaint?
If you are unhappy with anything through the course of taking part in the study, you can raise your concerns by asking to speak to a manager who will discuss matters with you and take any appropriate steps to resolve the situation. If you are still unsatisfied, you are entitled to complain by contacting Camden and Islington NHS Advice and Complaints Service:

Advice and Complaints Service
Camden and Islington NHS Foundation Trust
FREEPOST 1st Class (LON 12613)
London NW1 0YT
Tel: 020 3317 3117

What will happen to the results of the study?
The results will be written up as part of a thesis, which we hope will also be published in a scientific journal. A summary of the findings will be available to everyone who takes part.

Who is organising and funding the study?
The study is organised by University College London and Camden and Islington Foundation NHS Trust. Funding for the study is provided by University College London.

Contact for further information:
If you would like further information or have any questions, then please contact any of the researchers on:

Alternatively, you can leave a message for us at the Margarete Centre

Thank you for taking time to read this.

All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by National Research Ethics Service Committee South East Coast – Surrey.

Appendix D

Participant Information Sheet (control group (IAPT))

Camden and Islington NHS
NHS Foundation Trust

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London
WC1E 6BT

Tel:
Fax:

Participant Information Sheet
IAPT Participants

Study Title: Attention and Emotional Processes in Methadone- and Subutex-Maintained Opiate Users and Non-Users

Researchers: Matthew Charles (Trainee Clinical Psychologist), Clare Wellington (Trainee Clinical Psychologist) & Claire Mokrysz (PhD Student)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?

To understand how attention and emotions are involved in people's use of opiates like heroin. Research suggests that these processes may be important in why people become dependent on drugs, so we are looking at differences in attention and emotion between people who use opiates and people who don't.

Why have I been chosen?

We have asked you to take part because you are experiencing anxiety and/or depression, but are not using drugs of any kind.

Do I have to take part?

No, you do not have to take part in the study if you not wish to. If you are thinking of taking part you can keep a copy of this Information Sheet and you can contact us for more information if you wish. If you do decide to take part you can withdraw at any time without having to give a reason. Any decision you make will not affect your usual clinical care in any way.

What will happen if I take part?

We will arrange to meet with you on a single occasion the place where you receive your usual treatment. The meeting will last approximately 1.5 hours. During this time, you will have another chance to ask any questions you still have about the study. We will ask you some questions about your mental health and whether you regularly take drugs and you will be asked to complete a series of computer tasks and questionnaires. At the end of this we will give you £10 to compensate you for your time.

What will happen to my information?

All information collected about you during the study is strictly confidential and will be coded by number. Your name will not appear on any of the questionnaires you complete.

Camden and Islington NHS
NHS Foundation Trust

UCL

The only exception to this is if, during the course of the study, you disclose that you intend to harm yourself or other people. If this happens, we might speak to members of staff involved in your care to ensure that support is provided for you. Wherever it is possible, we would speak to you *first* to get your permission before speaking to anyone else.

What are the advantages and disadvantages of taking part?
We do not think that taking part will cause you distress. Some of the computer tasks you complete will involve looking at pictures of drugs and faces showing different emotions. There is a small chance you may experience a change in mood, but this would be temporary. Similar research that has been done in the past has never reported negative effects on those taking part. If in the unlikely event you do become distressed, you can let us know and appropriate support will be provided where necessary. We hope that the information we collect from this study will improve our understanding how people become and remain addicted to drugs. Through this, it is hoped this study will help to improve drug treatment services.

What should I do if I have a complaint?
If you are unhappy with anything through the course of taking part in the study, you can raise your concerns by asking to speak to a manager who will discuss matters with you and take any appropriate steps to resolve the situation. If you are still unsatisfied, you are entitled to complain by contacting Camden and Islington NHS Advice and Complaints Service:

Advice and Complaints Service
Camden and Islington NHS Foundation Trust
FREEPOST 1st Class (LON 12613)
London NW1 0YT
020 3317 3117

What will happen to the results of the study?
The results will be written up as part of a thesis, which we hope will also be published in a scientific journal. A summary of the findings will be available to everyone who takes part.

Who is organising and funding the study?
The study is organised by University College London and Camden and Islington Foundation NHS Trust. Funding for the study is provided by University College London.

Contact for further information:
If you would like further information or have any questions, then please contact any of the researchers on:

Alternatively, you can leave a message for us at reception.

Thank you for taking time to read this.

All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by National Research Ethics Service Committee South East Coast – Surrey.

Appendix E

Participant Information Sheet (control group (healthy))

Camden and Islington NHS
NHS Foundation Trust

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London
WC1E 6BT

Tel:
Fax:

Participant Information Sheet
Control Participants

Study Title: Attention and Emotional Processes in Methadone- and Subutex-Maintained Opiate Users and Non-Users

Researchers: Matthew Charles (Trainee Clinical Psychologist), Clare Wellington (Trainee Clinical Psychologist) & Claire Mokrysz (PhD Student)

You are invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please read the following information. Please ask us if there is anything that is unclear or if you would like more information. Take time to decide whether you wish to take part.

What is the purpose of the research study?

To understand how attention and emotions are involved in people's use of opiates like heroin. Research suggests that these processes may be important in why people become dependent on drugs, so we are looking at differences in attention and emotion between people who use opiates and people who don't.

Why have I been chosen?

We have asked you to take part because you are not using drugs of any kind.

Do I have to take part?

No, you do not have to take part in the study if you not wish to. If you are thinking of taking part you can keep a copy of this Information Sheet and you can contact us for more information if you wish. If you do decide to take part you can withdraw at any time without having to give a reason. Any decision you make is entirely voluntary.

What will happen if I take part?

We will arrange to meet with you on a single occasion at UCL. The meeting will last approximately 1.5 hours. During this time, you will have another chance to ask any questions you still have about the study. We will ask you some questions about your mental health and whether you take drugs and you will be asked to complete a series of computer tasks and questionnaires. At the end of this we will give you £10 to compensate you for your time.

What will happen to my information?

All information collected about you during the study is strictly confidential and will be coded by number. Your name will not appear on any of the questionnaires you complete.

Camden and Islington NHS
NHS Foundation Trust

UCL

The only exception to this is if, during the course of the study, you disclose that you intend to harm yourself or other people. If this happens, we might speak to other professionals to ensure that support is provided for you. Wherever it is possible, we would speak to you *first* to get your permission before speaking to anyone else.

What are the advantages and disadvantages of taking part?

We do not think that taking part will cause you distress. Some of the computer tasks you complete will involve looking at pictures of drugs and faces showing different emotions. There is a small chance you may experience a change in mood, but this would be temporary. Similar research that has been done in the past has never reported negative effects on those taking part. If in the unlikely event you do become distressed, you can let us know and appropriate support will be provided where necessary. We hope that the information we collect from this study will improve our understanding how people become and remain addicted to drugs. Through this, it is hoped this study will help to improve drug treatment services.

What should I do if I have a complaint?

If you are unhappy with anything through the course of taking part in the study, you can raise your concerns by speaking to the researcher who will discuss matters with you and take any appropriate steps to resolve the situation. If you are still unsatisfied, please contact the chief investigator:

H Valerie Curran
Professor of Psychopharmacology
Clinical Psychopharmacology Unit
University College London
Gower Street
London WC1E 6BT
0207 679 1898

What will happen to the results of the study?

The results will be written up as part of a thesis, which we hope will also be published in a scientific journal. A summary of the findings will be available to everyone who takes part.

Who is organising and funding the study?

The study is organised by University College London and Camden and Islington Foundation NHS Trust. Funding for the study is provided by University College London.

Contact for further information:

If you would like further information or have any questions, then please contact any of the researchers on:

Thank you for taking time to read this.

All proposals for research using human participants are reviewed by an ethics committee before they can proceed. This proposal was reviewed by the Research Department of Clinical, Educational and Health Psychology Ethics Chair, Project ID Number: CEHP/2013/503

Appendix F

Consent form (patient group)

Camden and Islington NHS
NHS Foundation Trust

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London
WC1E 6BT

Tel: 020 7679 1897
Fax: 020 7916 1969

Consent Form
Methadone- or Subutex-Maintained Participants

Confidential

Study: Attention and Emotional Processes in Methadone- or Subutex-Maintained Opiate Users and Non-Users

Name of researchers: Matthew Charles, Clare Wellington and Claire Mokrysz

I confirm that:	Please initial
1 I have read and understood the information sheet dated _____ for the above study	☐
2 I have had the opportunity to ask questions and discuss the study	☐
3 I understand I am free to withdraw from this study: • At any time • Without needing to give a reason • Without affecting my clinical care	☐
4 I agree to my most recent urine drug screen results to be made available to the researchers named above (optional)	☐
5 I agree to take part in the above study	☐

_____	_____	_____
Name of participant	Date	Signature of participant
_____	_____	_____
Name of researcher	Date	Signature of researcher

Appendix G

Consent form (control group (IAPT))

Camden and Islington NHS
NHS Foundation Trust

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London
WC1E 6BT

Tel
Fax

Consent Form
IAPT Participants

Confidential

Study: Attention and Emotional Processes in Methadone- or Subutex-Maintained Opiate Users and Non-Users

Name of researchers: Matthew Charles, Clare Wellington and Claire Mokrysz

I confirm that:	Please initial
1 I have read and understood the information sheet dated - _____ for the above study	☐
2 I have had the opportunity to ask questions and discuss the study	☐
3 I understand I am free to withdraw from this study: • At any time • Without needing to give a reason • Without affecting my clinical care	☐
4 I agree to take part in the above study	☐

_____	_____	_____
Name of participant	Date	Signature of participant
_____	_____	_____
Name of researcher	Date	Signature of researcher

Appendix H

Consent form (control group (healthy))

Camden and Islington NHS
NHS Foundation Trust

Doctorate in Clinical Psychology (DClinPsy)
Research Department of Clinical, Educational & Health Psychology
University College London
1-19 Torrington Place
London
WC1E 6BT

Tel:
Fax:

Consent Form
Control Participants

Confidential

Study: Attention and Emotional Processes in Methadone- or Subutex-Maintained Opiate Users and Non-Users

Name of researchers: Matthew Charles, Clare Wellington and Claire Mokrysz

I confirm that:	Please initial
1 I have read and understood the information sheet dated - _____ for the above study	☐
2 I have had the opportunity to ask questions and discuss the study	☐
3 I understand I am free to withdraw from this study: • At any time • Without needing to give a reason	☐
4 I agree to take part in the above study	☐

_____	_____	_____
Name of participant	Date	Signature of participant
_____	_____	_____
Name of researcher	Date	Signature of researcher

Appendix I

NHS REC ethical approval letter

NHS
Health Research Authority
NRES Committee South East Coast - Surrey
HRA
Research Ethics Committee (REC) London Centre
Ground Floor
80 Skipton House
London Road
London
SE1 6LH

Telephone:
Facsimile:

10 September 2012

Professor Val Curran
Professor of Psychopharmacology
Clinical Psychopharmacology Unit
University College London
Gower Street
London
WC1E 6BT

Dear Professor Curran

Study title: An Investigation Into Attentional Bias and Recognition of Emotional Facial Expressions in Methadone-Maintained Opiate Users and Non-Users

REC reference: 12/LO/1075

Thank you for your letter of 24 August 2012, responding to the Committee's request for further information on the above research and submitting revised documentation

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Covering Letter		19 June 2012
Evidence of Insurance or Indemnity		15 August 2011
Investigator CV	Val Curran	
Other: CV: Dominic O'Ryan		
Other: CV: Clare Wellington		
Other: CV: Matthew Charles		
Other: Control Group Flow Chart	1	22 March 2012
Other: Patient Group Flow Group	1	22 March 2012
Other: Participant Information	1	30 March 2012
Other: Advertisement: Are you prescribed methadone?	1.0	30 March 2012
Other: Research Proposal Review Form: John King		06 October 2011
Other: Research Proposal Review Form: John King		09 February 2012
Other: Advertisement: Are you feeling low or anxious?	2.0	20 August 2012
Participant Consent Form: Control	1.0	22 March 2012
Participant Consent Form: Methadone Maintained	1.0	22 March 2012
Participant Information Sheet: Methadone Maintained	2.0	20 August 2012
Participant Information Sheet: Control	2.0	20 August 2012
Protocol	1	01 February 2012
REC application	96386/335665/1/24	19 June 2012
Response to Request for Further Information		24 August 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for

Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/LO/1075	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

pp
Prof David Russell-Jones
Chair

Email: NRESCommittee.SECoast-Surrey@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: Mr Dave Wilson, UCL
Mrs Angela Williams, Camden & Islington NHS Foundation Trust

Appendix J

UCL PaLS ethical approval letter

DIVISION OF PSYCHOLOGY AND LANGUAGE SCIENCES

UCL

Ethics Application Form for Non-Invasive Research on Healthy Adults

SECTION A APPLICATION DETAILS

A1 Project details

Project title: Attention and Emotion in healthy volunteers

Date of submission: 19/04/2013

Proposed start date: 1/05/2013

Proposed end date: 31/12/2019

A2 Principal researcher

(Note: A student – undergraduate, postgraduate or research postgraduate – cannot be the principal researcher for ethics purposes).

Full name: Prof Val Curran

Position held: Professor of Psychopharmacology

Research Department: Clinical Psychopharmacology Unit

The principal researcher must read and sign (electronic signature or scanned pdf with signature are acceptable) the following declaration. Please tick the box next to each of the statements below to acknowledge you have read them and provided all required information.

♣ I will ensure that changes in approved research protocols are reported promptly and are not initiated without approval by the Departmental Ethics Committee, except when necessary to eliminate apparent immediate hazards to the participant.	x
♣ I have completed a risk assessment for this programme of research and hereby confirm that the risk assessment document will be discussed with any researcher/student involved in this programme of research (currently or in the future). I will ensure that all researchers/students sign the risk assessment form following this discussion. **Risk assessment forms for projects can be downloaded from the Ethics section of the PaLS Intranet.**	x
♣ I have obtained approval from the UCL Data Protection Officer stating that this research project is compliant with the Data Protection Act 1998. My Data Protection Registration Number is: Z6364106/2012/02/33 You can find a data protection registration form here: http://www.ucl.ac.uk/efd/recordsoffice/data-protection/	x
♣ I have included examples of the Information Sheet and Consent Form for the proposed research. It will be made clear to the participants that they can withdraw from the study at any time, without giving a reason.	x
♣ I will ensure that all adverse or unforeseen problems arising from the research project are reported in a timely fashion to the UCL Research Ethics Committee.	x
♣ I will undertake to provide notification when the study is complete and if it fails to start or is abandoned.	x
♣ I have met with and advised students on the ethical aspects of this project/programme of research.	x
♣ I am satisfied that the proposed research complies with current professional, departmental and university guidelines.	x

Signature: **Date: 27-4-13**

A3 Contact details

Principal Researcher

Full name: Prof Val Curran

Position held: Professor of Psychopharmacology

Research Department: Clinical Psychopharmacology Unit

Email: [redacted] Telephone: [redacted]

Additional applicant 1

Full name: Matthew Charles

Position held: Trainee Clinical Psychologist

Research Department: Research Department of Clinical, Educational and Health Psychology

Email: [redacted] Telephone [redacted]

Additional applicant 2

Full name: Clare Wellington

Position held: Trainee Clinical Psychologist

Research Department: Research Department of Clinical, Educational and Health Psychology

Email: [redacted] Telephone: [redacted]

(Add further details on a separate sheet if there are more applicants to be covered by this form)

A4 Approval from the Departmental Ethics Committee

(Approval cannot be given by the principal researcher of this project – if necessary the application must be sent to an Ethics Officer from a different Research Department, or to the College Ethics Committee, for approval)

Declaration by the Research Department Ethics Chair:

I have reviewed this project and I approve it. ☐

The project is registered with the UCL Data Protection Officer and a formal signed risk assessment form has been completed.

Allocated Departmental Project ID Number for the approved application:

_ CEHP/2013/503 _

Name of the Research Department Ethics Chair (type in): Dr John King

Date: 3rd May 2013

2

Appendix K

Barratt Impulsiveness Scale-11

Patton, Stanford, Barratt (1995). *J Clin Psy*, vol. 51, pp. 768-774

Appendix L

Visual Analogue Scales Used

Pp # ☐ Visit # ☐

Please place a line (|) on the lines below to show how you are feeling AT THIS MOMENT IN TIME:

I would like to use drugs

Not at all Extremely

I want to use drugs

Not at all Extremely

I have an urge to use drugs

Not at all Extremely